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 MASSIVE DOSAGE OF INTRAMUSCULAR LIVER EXTRACT IN THE TREATMENT OF PERNICIOUS ANÆMIA.			
 By HILDA J. GARDNER, M.B., B.S., <i>Clinical Pathologist, Melbourne Hospital,</i>			
AND			
IAN J. WOOD, M.D., M.R.C.P., <i>Associate Assistant, Melbourne Hospital; Honorary Physician to Out-Patients, Children's Hospital, Melbourne.</i>			
(From the Walter and Eliza Hall Institute, Melbourne.)			
 CASES of severe pernicious anæmia with erythrocyte counts of one million or less call for such treatment as will most readily evoke an adequate response.			
The mental condition of such patients may present a problem to the physician. Many cases are on record in which the patient has resolutely refused			
 to enter a hospital or to submit to any treatment whatsoever. Patients in severe relapse also suffer from severe anorexia, very often associated with vomiting and diarrhoea, which precludes the ingestion of adequate amounts of whole liver. Parenteral administration would therefore seem to be the method of choice. A single large dose of a potent extract will almost invariably change the mental attitude to one of sanity and cooperation in from five to ten days, as well as putting the patient on the high road to recovery.			
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To Gänsslen⁽²⁾ belongs the credit of first pointing out in 1930 the advantages of parenteral over oral administration and of preparing a suitable extract for the purpose. It has been variously estimated

that the effectiveness of parenteral injection is 30 to 100 times that of liver taken by mouth. Davidson⁽³⁾ and Wilkinson⁽⁴⁾ were among the early users of this concentrated principle, and both report cases treated successfully in this manner.

Riddle and Sturgis,⁽⁵⁾ working with liver extracts given by mouth, confirmed Minot's opinion that the response depends on the total amount of active liver principle available in a given time rather than on the amount consumed each day, the effect of a given amount lasting a given time, whether administered in one or divided doses. Riddle and Sturgis also showed that the magnitude of the reticulocyte response was not influenced by the presence of excessive amounts of active liver principle in the body. The maximum response has a definite fixed level, which varies inversely as the erythrocyte count at the beginning of treatment—the lower the count, the higher the reticulocyte response. The attainment of this maximum is, however, accelerated by the use of collective doses. These principles of storage and reticulocyte response are also applicable to parenteral administration.

Lendvai⁽⁶⁾ has used single doses of twenty cubic centimetres of a potent extract followed by a further dose after a variable period depending on individual requirements with very satisfactory results, remission lasting three months or longer after one or two such injections.

This report of three cases of pernicious anaemia in severe relapse, selected from a series treated with massive doses of liver extract given intramuscularly, demonstrates the early clinical and haematological response to such treatment. A pleasing feature of this method to both patient and physician is the limited number of injections required, no one needing a daily intramuscular injection.

The extract selected for use was "Campolon",¹ and very little, if any, local reaction and no general reaction followed the use of large doses. As soon as the diagnosis was confirmed, a preliminary dose of four cubic centimetres was given to exclude the possibility of any abnormal sensitivity, and this was followed within twelve hours by a further dose of twenty cubic centimetres.

Daily reticulocyte estimations during the first week are necessary as a guide to an effective response. Efficient treatment manifests itself as a rapid rise in the reticulocyte count which appears before any demonstrable increase in the erythrocyte count or haemoglobin percentage. Progress must be followed from the end of the first week by bi-weekly haemoglobin estimations and erythrocyte counts as a guide to further therapy. The amount required varies greatly in individual patients.

Throughout the following investigations the standard ward diet was given. This did not include any liver or special foods containing anti-anæmic factors.

The method used in counting the reticulocytes was as follows: A saturated alcoholic solution of brilliant cresyl blue was spread on a clean warm

slide, where it rapidly dried, leaving a fine film of dye. A blood film was smeared on this surface and stained with Leishmann stain in the usual manner. The percentage of reticulocytes occurring amongst 500 to 1,000 red cells was determined with the aid of a micrometer disk in the eyepiece of the microscope.

In our experience the average time for the maximum reticulocyte response to occur is as follows: (a) Intramuscular massive dose ("Campolon", twenty cubic centimetres)—two to five days. (b) Intramuscular small divided doses ("Campolon", two to four cubic centimetres daily)—four to eight days. (c) Oral administration of fresh liver or extracts—six to ten days.

Case Histories.

CASE I.—I.C., a female, aged sixty years, was admitted to the Melbourne Hospital on May 30, 1934, under the care of Dr. Hume Turnbull. Three years previously she had been treated at another hospital in Melbourne for pernicious anaemia. Since then she had been taking liver and hydrochloric acid by mouth, but for several months prior to admission she had taken a dried liver extract and no fresh liver. In spite of this she had become progressively weaker in the last four months. (This extract may have been inactive or the absorption from the alimentary canal may have been at fault.) Dyspnoea even at rest had been severe, and swelling of the ankles, tingling and numbness in the limbs and inability to sleep had become marked features.

The patient looked old and extremely pale. There was gross orthopnoea and prostration. Death appeared to be imminent. The temperature was 36.1° C. (97° F.), the pulse rate was 100, and respirations numbered 24 in the minute. The heart was enlarged, with a blowing systolic bruit at the apex. The systolic blood pressure was 102 and the diastolic pressure 85 millimetres of mercury. The lungs were not congested and the abdomen showed no enlargement of the viscera. There was a severe grade of pernicious anaemia, the red cell count being 920,000 per cubic millimetre and the haemoglobin 20% (Sahli) (see Table I). "Campolon", in a dose of twenty cubic centi-

TABLE I.
Summary of Investigations Prior to the Beginning of Treatment.

Test.	Normal.	Case I.	Case II.	Case III.
Hemoglobin (Sahli, 17 grammes—100%) ..	80%	20%	16%	27%
Red cells ..	5,000,000	920,000	780,000	1,080,000
Colour index ..	0.8	1.1	1.0	1.3
Red cell diameter (Eve's halometer) ..	7.2 μ	8.1 μ	Not tested.	Not tested.
Reticulocytes ..	0.5%	1%	Nil.	Nil.
Anisocytosis ..	Nil.	+++	++	+++
Macrocytosis ..	Nil.	+++	++	+++
Poikilocytosis ..	Nil.	++	Slight.	++
Polychromasia ..	Nil.	+	0	+
Nucleated red cells ..	Nil.	Occasional.	Occasional.	Nil.
Leucocytes ..	5-10,000	6,150	1,300	6,500
Neutrophilic polymorphonuclear cells ..	63%	54%	28%	52%
Eosinophilic polymorphonuclear cells ..	3%	Nil.	Nil.	1.2%
Monocytes ..	6%	3.5%	6%	2%
Lymphocytes ..	23%	30-5%	66%	1.5%
Fouchet test ..	Negative.	Positive.	Not tested.	42.5%
Van den Bergh test ..	0.5-1.0 unit.	4.5 units.	Not tested.	Not tested.
Fractional test meal ..	Free acid present.	Absent free acid.	Absent free acid.	Absent free acid.

metres, was injected intramuscularly twelve hours after a preliminary dose of four cubic centimetres had produced no deleterious local or general reaction. The resulting rise in the reticulocytes, red cells and haemoglobin is shown in Figure I.

¹ Made by Bayer Products, Limited.

The clinical response was dramatic, slight improvement being noticed in twenty-four hours, and marked improvement in forty-eight hours. The mental torpor and confusion cleared in about five days and the patient returned to a state of excellent health and strength. A normal blood picture was reached a month after admission, two injections only being required to obtain this level.

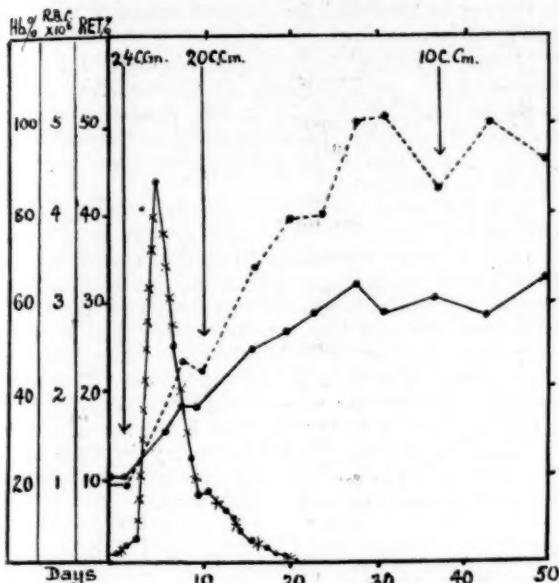


FIGURE I.

Showing the early and abundant reticulocyte response and rapid rise in red cells and haemoglobin after intramuscular administration of liver extract (Case I). The cubic centimetre doses represent doses of "Campolon". The uninterrupted line represents haemoglobin percentage; the interrupted line represents red blood cells per cubic millimetre; the uninterrupted line with crosses represents reticulocyte percentage.

This patient lives in the bush far from medical aid, where a regular supply of fresh liver is difficult to obtain. Once a month, when she pays her periodic visit to the nearest township, she visits her doctor and receives eight cubic centimetres of "Campolon" with but slight discomfort, and in this fashion she has maintained a perfect state of sanguination and well-being for many months.

It is of interest to record that in order to restore the haemoglobin to normal it was necessary to administer iron by mouth.

CASE II.—E.D., a female, aged fifty-two years, was admitted to the Melbourne Hospital under the care of Dr. Lawton. One year previously she had been effectively treated for pernicious anaemia with divided doses of "Campolon" given intramuscularly and liver given orally. On discharge she had been advised to continue on liver by mouth. When readmitted on October 7, 1934, it was stated that she had had no treatment for several months, the chief reason being that ill-fitting dentures had produced an ulcerated mouth. This was followed by glossitis attending the relapse. She became too weak to attend the out-patient department, and when admitted was *in extremis*, being semi-comatose and grossly anaemic. Her skin had an icteric tinge and there were purpuric spots on the flexor surfaces of both forearms.

The red cell count was 780,000 and the haemoglobin 16% (Sahli) (see Table I). The tongue was dry, red and glazed. The pulse rate was 120 and respirations numbered

24 in the minute. The heart was moderately enlarged, with a soft mitral systolic bruit. In the lungs there was basal congestion with crepitations, and the abdomen showed no abnormality, the spleen being impalpable.

"Campolon", four cubic centimetres, was given intramuscularly and, as there were no local or general reactions, twenty cubic centimetres were injected twelve hours later. On the following day a small blood transfusion of 180 cubic centimetres (six ounces) was given, together with 240 cubic centimetres (eight ounces) of normal saline solution. This was followed twenty hours later by 1.8 litres (three pints) of saline solution given by the rectum.

On the third day after the first dose of "Campolon" the patient gradually began to recover from her moribund condition, and by the end of three weeks she had made remarkable improvement. The temperature remained elevated for a fortnight, but this was considered to be due mainly to a mild static bronchopneumonia. However, a moderate degree of pyrexia is not uncommon with profound anaemia.

The injections of "Campolon" and the resulting rise in reticulocytes, red cells and haemoglobin are shown in Figure II.

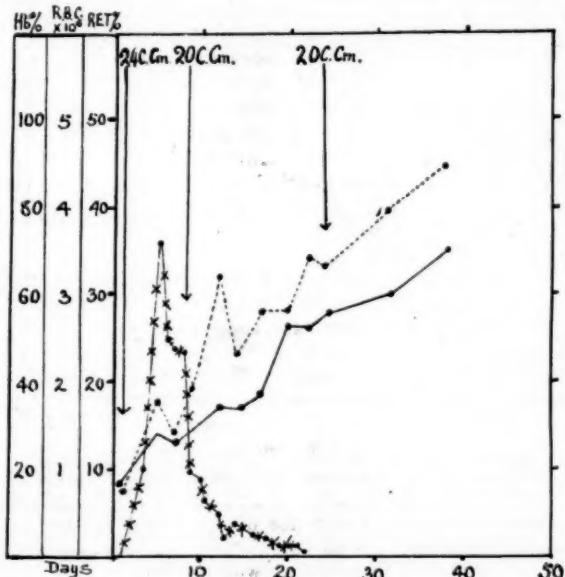


FIGURE II.

Showing the rapid reticulocyte response in Case II. A transfusion of 180 cubic centimetres (six ounces) of blood was given on the fourth day. The cubic centimetre doses represent doses of "Campolon". The uninterrupted line represents haemoglobin percentage; the interrupted line represents red blood cells per cubic millimetre; the uninterrupted line with crosses represents reticulocyte percentage.

It will be noted that in this case only three massive doses were required for complete remission.

CASE III.—J.C., aged forty-eight years, a storeman, was admitted to Melbourne Hospital on September 11, 1934, under the care of Dr. Ivan Maxwell. Four weeks earlier his legs had begun to swell and he noticed increasing pallor, weakness and shortness of breath on exertion.

Two weeks before his admission to hospital a cough developed with a small amount of sputum. He thought that he had been losing weight for about a year, otherwise his previous health had been good.

The patient was a tall, thin man with a lemon-tinted skin, who lay propped up in bed. He appeared to be grossly anaemic. His mental condition was greatly disturbed. He was restless, alert and resented any form of treatment, asserting vigorously that he was not ill. The temperature

was 36.7° (98° F.), the pulse rate was 82 and respirations numbered 22 in the minute. The lungs showed bronchitis, the heart was slightly enlarged, and examination of the abdomen revealed no abnormality, the spleen being impalpable. There was no swelling of the ankles. The laboratory examinations (see Table I) showed the typical picture of pernicious anaemia, the red cells numbering only 1,080,000 and the haemoglobin value being 27%. Treatment was begun with intramuscular injections of "Campolon". An initial dose of four cubic centimetres was administered and, as there was no reaction, a further dose of twenty cubic centimetres was given twelve hours later. The subsequent injections and the response of the reticulocytes, red cells and haemoglobin are shown in Figure III.

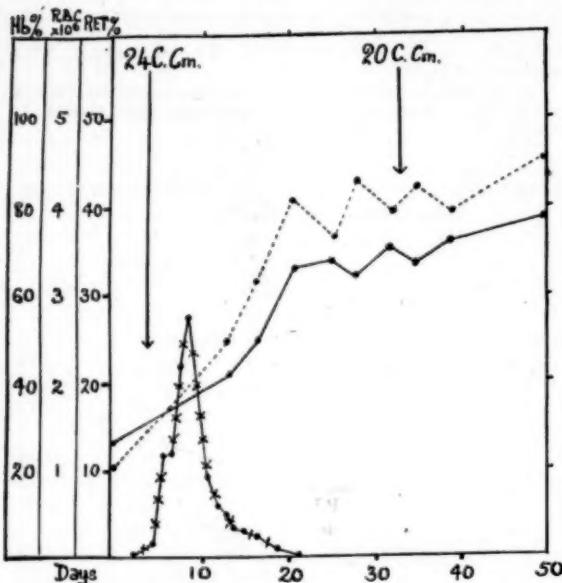


FIGURE III.

Showing the rapid response to intramuscular injections of liver extract in massive doses (Case III). Note the time interval between the first and second doses. The cubic centimetre doses represent doses of "Campolon". The uninterrupted line represents the haemoglobin percentage; the interrupted line represents red blood cells per cubic millimetre; the uninterrupted line with crosses represents reticulocyte percentage.

So dramatic was the response in this case that within a fortnight he was transformed from a mentally confused man of deathly pallor to a sane cooperative individual with the normal pink colour already reappearing in his cheeks. The routine blood examinations after the return of the blood picture to normal showed that the second dose of twenty cubic centimetres of "Campolon" maintained the red cells and haemoglobin within normal limits for three months (see Figure IV). No anti-anæmic factor in any form was given during this period and his general health was excellent.

Comment.

The most important reason for preferring the massive intramuscular injection of liver extract for the treatment of severe cases of pernicious anaemia is the rapidity of its action. An earlier response is claimed for intravenous liver therapy, but of this we have had no experience. These patients are in

imminent danger, so the time factor is all important; the quicker the response, the better the method. As the reticulocyte response is the first indication of improvement, preceding the rise in haemoglobin and red cells, the interval between the onset of treatment and the maximum reticulocyte response is the key to assessing the relative values of various therapeutic measures.

If the expected reticulocyte response fails to appear, then the possibility of an incorrect diagnosis, a faulty technique in the counting of the reticulocytes (especially the quality of the brilliant cresyl blue solution) or a non-potent liver extract should be considered.

With the extract used the response has been consistent and local and general reactions have been negligible. After the initial injections, amounting to twenty-four cubic centimetres, the indication for further treatment is afforded by observing the level of the red cells and haemoglobin. There is no uniformity with different individuals, as is shown in the three cases reported in the present series. Here the second injection of twenty cubic centimetres was given on the ninth day in Case I, the seventh day in Case II, and on the thirtieth day in Case III. We have not found that any of our cases needed further therapy during the first week.

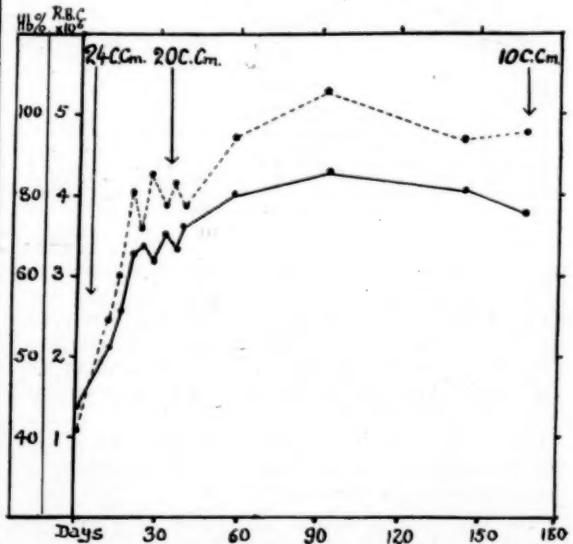


FIGURE IV.

Showing the prolonged response to massive intramuscular doses of liver extract (Case III). The cubic centimetre doses represent doses of "Campolon". The uninterrupted line represents haemoglobin percentage (Sahli); the interrupted line represents red blood cells per cubic millimetre.

Maintenance Dose.—Once a normal level is established, a plan of treatment must be decided upon. This is a very interesting problem, which is outside the scope of this paper. Suffice it to say that the treatment of pernicious anaemia with depot doses alone is rapidly gaining favour. In Case III in our series the patient maintained a normal red cell

count and haemoglobin percentage for three months after the second injection of twenty cubic centimetres (Figure IV). Patients may have four to ten cubic centimetres injected once a month, according to their individual requirements, or it may be more convenient to give larger doses less frequently.

During the second week of treatment of a patient with pernicious anaemia the colour index drops below unity, as the red cells are always replaced more rapidly than the haemoglobin. At this early stage the iron stores of the body are still rich following the haemolytic processes which have taken place prior to treatment. However, with the rapid synthesis of haemoglobin these stores may be exhausted before a normal picture is restored. If so, iron in large doses should now be administered by mouth, preferably iron and ammonium citrate in doses of 5·4 grammes (ninety grains) daily. When pernicious anaemia is treated with whole liver by mouth, this iron deficiency does not tend to occur, owing to the high iron content of liver.

In view of the rapid response which can now be expected in severe cases of pernicious anaemia, blood transfusion is becoming less necessary. It should be borne in mind that in these cases there is a definite element of risk in performing a transfusion, no matter how thoroughly the blood grouping is carried out.

In conclusion, it must be stressed that the object of any treatment of pernicious anaemia should be, first, to bring the red cell count and haemoglobin percentage back to normal as rapidly as possible and, secondly, rigidly to maintain this state of normality. Any treatment which fails to carry out these principles is inefficient. In our opinion, massive intramuscular doses of liver extract produce the most rapid response, and depot doses are an efficient method of maintaining a normal blood picture.

We are in agreement with Dameshek and Castle,⁽⁷⁾ who state that "the parenteral method is more regular in its effectiveness, less expensive to the patient, certainly easier to tolerate than continual oral administration, and more amenable to careful supervision by the physician".

Summary.

1. The problems which arise during the treatment of severe pernicious anaemia are discussed.

2. The pioneer work on the isolation and intramuscular injection of the active principle of liver is described.

3. Effective treatment is judged by an early reticulocyte response. Further injections are given when the haemoglobin and erythrocyte levels begin to fall.

4. Three cases of pernicious anaemia are reported with erythrocyte counts of a million or less, and the response to massive intramuscular doses of liver extract ("Campolon", twenty-four cubic centimetres) is shown.

5. The maintenance dose is briefly discussed, with special reference to depot doses given intramuscularly.

Acknowledgements.

We are indebted to those members of the honorary staff of the Melbourne hospital who placed the cases at our disposal and gave invaluable advice; to Dr. Ivan Maxwell, who made the first supplies of "Campolon" available to the hospital; and to Dr. Charles Kellaway, for his untiring help and constructive criticism.

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RECORD OF LAST YEAR'S WORK AT THE HOBART INFECTIOUS DISEASES HOSPITAL (VAUCLUSE).¹

By C. N. ATKINS, M.B., Ch.B. (Melbourne),
D.P.H. (Oxon).

Superintendent, Infectious Diseases Hospital; Medical Officer of Health, Hobart.

I THOUGHT that tonight we might review the year's work at Vaucluse Infectious Diseases Hospital up till November, 1934, especially as Tasmania has a bad diphtheria rate. Our case incidence yearly average for the ten years to 1932 was 42·7 per 100,000. Bendigo had an incidence of 42·1, but the Adelaide incidence was only 1·9. In Melbourne the incidence was 20·5, and in this connexion, as I have pointed out before, it is interesting to note that before the immunization campaign was started in Melbourne the rate was about 34 and that but for a couple of bad years in 1931 and 1932 the rate of 20·5 would have been less still. Even so, that rate was less than the rate of some surrounding municipalities, which fared worse in the epidemic because immunization had not been carried out.

Perth has a good rate (3·6) and Launceston's figures, 28·5, are better than ours. However, I do not think that our rate is as bad as it looks, for we shall find that we are branded with a lot of cases that are not diphtheria at all, and incidentally, too, in those cases which are diphtheria the patients came into hospital very late during this last year, and this, of course, has affected our death rate.

¹ Read at a meeting of the Tasmanian Branch of the British Medical Association on February 12, 1935.

The total number of patients admitted into the Vaucluse Hospital was 294. These came from Hobart and the eighteen neighbouring municipalities, with which we have an agreement to treat their patients. Practically all patients notified are treated at Vaucluse.

Now, of the 294 patients, I marked 59 on admission as not suffering from clinical diphtheria. Of these 19 gave subsequent positive swabs and 40 "negative". So that nearly one in seven infections was not diphtheria at all, as 40 out of the 294 patients could reasonably be said not to have had it.

Of course one cannot blame the medical man who, especially in the country, takes the safe course and sends patients to Vaucluse rather than leave them isolated in the bush. But I cannot find out similar figures for other hospitals with a view to forming an estimate as to whether or not we are being credited with more cases in Tasmania than we deserve. This question of diagnosis becomes more difficult to me the more I see of it.

There are, of course, the definite cases, one way or the other, but it is the indefinite case which is so misleading. I used to follow Ker's old rule, that if you see more than one spot on any area, it is not diphtheria, but I find that one cannot rely on it. I have often seen the typical spots of follicular tonsillitis run together by the next morning and the patients give a positive swab, so that I personally find little use in that rule. The peculiar acrid smell is more helpful, but I have come to rely much more upon the general appearance of the patient apart from the throat.

I may be wrong, but my growing impression is that diphtheria patients are pale in the face and look much more ill than the non-diphtheritic patients. The flushed, red, feverish child does not seem to be suffering from diphtheria. The pale, sick, listless child does.

The question of swabs without a virulence test, I need hardly tell you, is most misleading, particularly in branding people as carriers. In a bad case a "negative" swab is often obtained, and I almost wish there were no swabbings, so misleading are they. Just to show this, of the 235 patients who on admission were marked "clinical diphtheria", 99 subsequently had "negative" swabs and 136 positive.

The interesting thing about Tasmania is the absence of laryngeal diphtheria. There were only six cases out of the 294, and of these, four only gave positive swabs. Personally I doubt if any of them were diphtheritic laryngitis, and certainly none of the patients was seriously ill. One of them died, but this patient definitely had double pneumonia.

Now to consider the deaths that took place. There were 14 deaths in 294 cases, that is, 5.1%. In 1928 the percentage death rate among cases was 6.3. In 1932 the percentage death rate among cases was 1.5. In 1933 the percentage death rate among cases was 2.2.

Of the fourteen patients who died, two died about one hour after admission—one on the doorstep. Five

died on the second day. One had a long struggle for forty days.

The worst feature of these deaths, of course, is that only one patient came in on the first day of illness. Only one came in on the second day, and nine on the third day of the illness. Four came in on the fourth and fifth days of the illness. So that of the children whom we got on the first day, only one died out of 294.

It is also interesting to see how long most of the other children who lived had had the illness before they came to hospital. Of the 294 patients admitted, only 91 came on the first day. Fifty-four came on the second day, that is, 145 for the first and second days and 149 after the second day.

These figures tell their own story. Of course, the people do not do it deliberately, but it is a great pity they are not more careful to send for the doctor earlier. The doctors themselves are not to blame; it is very rarely indeed that they have delayed; mostly they err on the side of caution.

And just while on this subject I should like to point out again that patients cannot be admitted into Vaucluse with an order signed "suspected diphtheria". You see, we take in patients for the municipalities on a written order saying that the patients are suffering from an infectious disease. If the municipalities liked to ask us to take in "suspected" cases, we should do so with pleasure, but they have not done so because they are not bound to provide for contacts or suspects, as they are bound to do for certified cases. If we started to take everything in, the municipalities would soon object to paying the bill.

Now with regard to the treatment of these patients who die. Unfortunately I have not been able to find out anything fresh. Death takes place from a vasomotor failure or a myocardial failure. It is known that the vasomotor failure is peripheral and not altogether central. My attention was drawn by Dr. Sprent to an article in *The Lancet* describing the advantages of total immersion in a warm bath, as in typhoid fever. I tried to get some more literature on the subject, but failed to do so, and so far I have not had the courage to lift a dying child into a bath.

You all know the symptoms we meet—vomiting, epigastric pain, pallor, low blood pressure, pain over the heart, restlessness and death. I can find no advice anywhere, except to give the antitoxin earlier. I have tried big doses intravenously, but it is too dangerous. As one authority on this subject told me: "If you give sedatives you kill them; if you give stimulants you kill them; so you might as well let them die in peace."

We have had patients get better after the whole broadside of stimulants—glucose, strychnine, "Coramine", pituitrin, adrenaline, camphor, all given in desperation—and, conversely, patients who have got better without anything. I think it sounds sensible to give glucose from the start, in preparation for these collapses, and we always give the patients,

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Immunization has been carried out here for the year, but under difficult conditions. We have not been able to persuade the Government to take it on on a large scale. It has had to be done amongst institutions and the public wherever we got the chance. The nurses at the General Hospital and Vaucluse, and the inmates at the Boys' Home and the Girls' Industrial School have all been done free of charge. Nobody yet amongst those immunized has had diphtheria. The Boys' Home was a good example. The Sub-Matron was away when the place was gone through. She came back and developed diphtheria. Two of the boys gave positive swabs but did not develop the disease, which was gratifying. Nobody else suffered from it.

THE DETECTION OF HYPERSENSITIVENESS.

By CHARLES SUTHERLAND, M.B., M.R.C.P.,
*Honorary Physician to Asthma Clinic, Alfred
Hospital, Melbourne.*

(From the Baker Institute of Medical Research.)

HYPERSENSITIVENESS to certain pollens, dusts and foods is becoming increasingly recognized as an important factor in the so-called allergic diseases. Skin tests offer an easy method of detecting this hypersensitivity, but a certain amount of care is necessary in doing these if misleading results are to be avoided.

The Importance of History.

Before any tests are done, it is essential to take a detailed history. A patient hypersensitive to some dust or pollen in his surroundings almost invariably reports that he is afflicted only in certain seasons or certain localities. If symptoms are quite unaffected by season or environment, one usually finds that intrinsic factors, such as sepsis or metabolic or digestive abnormalities, are of more importance. Frequently the patient will have a fairly accurate idea himself and will save the physician much time by indicating that horse dander, feather pillows or certain flowers or foods upset him. But even when he is certain that one factor causes symptoms, it is always wise to test with all the other commonly recognized causes. For instance, a patient sensitive to horse dander may fail to get satisfactory relief from desensitization because a coincident sensitiveness to kapok had been missed. On the other hand, if a patient with perennial symptoms reacts only to spring pollens, one can be fairly certain that some other factor has been missed.

The Types of Reactions.

Two main types of reaction are commonly recognized: (a) the immediate urticarial wheal reaction, typified fairly well by a mosquito bite, and (b) the

slowly developing erythematous "patch test" reaction, which is comparable in some ways with the von Pirquet test. The former appears in seven to fifteen minutes, and the latter in one to three days. The patch test is used almost exclusively in studying cases of "contact dermatitis".

It is well recognized that hypersensitivity is usually easily transferable passively. A few drops of serum from a hypersensitive donor injected intradermally into a non-sensitive recipient passively sensitizes a patch about three centimetres in diameter. This passive sensitization is established within twenty-four hours of injection and may persist for months. The quality in the serum conveying this sensitiveness is known as "reagin".

Reagents.

Quite crude preparations are often very potent reagents. For instance, a little dander from a horse, moistened and rubbed into a scratch on a patient sensitive to horses, will produce a large wheal; but, of course, the risk of infection makes it advisable to use more refined preparations. As a rule the best method is to wash the finely ground substance in several changes of perfectly dry ether to remove all fat. Allow the ether to evaporate and then extract with a buffered saline solution, such as "Cocas solution". Glycerine has an excellent stabilizing effect, and often it is advantageous to use equal parts of "Cocas solution" and glycerine. Many reagents keep better in the dry state, and better reactions are obtained with them if they are dissolved just before application to the scratch. Pollens should always be kept in the dry state and applied as a freshly prepared paste. Linseed should be washed in several changes of ether and kept as a dry powder for testing. Orris root and pyrethrum seem better if used as purchased without any washing. When testing with foods such as egg white, often it is best to test with the fresh untreated foods. However, it is often inconvenient to get together a large number of fresh samples of foods, and then the best plan is to prepare a paste by mashing the food with a little boric acid powder and adding enough glycerine to make it into a thin paste. Some vegetables prepared in this way rapidly lose their power to produce skin reactions, but others keep for a surprisingly long time. For instance, a walnut extract prepared in this way four years ago still produces reactions as large as freshly made pastes. Liquid extracts of most vegetables, meats and other foods usually throw down precipitates and become inert. It may be said that as yet no really satisfactory method of preparing foods for testing has been found, and that generally, for scratch tests, it is best to use fresh samples or freshly made pastes. For intradermal tests freshly made sterile liquid extracts are, of course, essential; but it is probable that in most cases of sensitiveness as good a reaction is given by applying the fresh food to a scratch as by intradermal tests with the necessarily refined and attenuated liquid extracts.

The following reagents are commonly used in testing:

Epithelia and Dusts.—Horse dander, dog hair, hen feathers, cat hair, goose feathers, rabbit fur, cattle hair, goat hair, duck feathers, sheep's wool, house dust, mouse hair, kapok, Le Page's glue, pyrethrum, orris root, linseed, silk, cotton seed, mould, castor oil bean.

Pollens.—Iceland poppy, capeweed, sunflower, prairie grass, sweet pea, sorrel, rye grass, dahlia, dock, cocksfoot, cosmos, plantain, *Poa annua*, Kentucky blue, couch grass, pine tree, wattle, *Bromus mollis*, canary grass, paspalum grass, Yorkshire fog grass, ragweed, Timothy grass, oat, sweet vernal, red top.

Foods.—Egg white, milk, chicken, pork, beef, lamb, whitening, oatmeal, wheat, bean, tomato, almond, cabbage, potato, barley, coffee, lentil, green pea, rice, banana, Brazil nut, maize, lettuce, honey, onion, walnut, tea, mustard, rye, spinach, pepper, celery, orange, chocolate, coconut, pineapple, peanut, sultana, currant, sago, parsley, crayfish, rhubarb.

Apparatus.

Reagents are best kept in small rubber-stoppered homoeopathic phials of about two cubic centimetres capacity. Woodsen trays bored with holes arranged to hold two rows of ten can be made cheaply. One tray can contain about seventeen of the perennial factors which cause asthma and hay fever—horse dander, feathers, kapok *et cetera*—and it is convenient to have also in this tray tubes containing one cubic centimetre of human tuberculin, bovine tuberculin, and a control fluid for the von Pirquet test. A moderately sharp scalpel is kept in a wide-mouthed bottle containing lysol, 1 in 20, with a pad of wool at the bottom to protect the blade. A set of applicators for applying reagents should also be made. These are similar to the platinum loops used for bead tests in chemical analysis. They are best made of three-inch lengths of the wire used in electric radiators (Nicrom wire). Fairly heavy gauge is used, and a neat loop is made at the end for applying liquid reagents. Others should have the end flattened on an anvil to form tiny spatulae for application of powders. These wires are fixed into three-inch lengths of glass rod.

Performing the Tests.

The patient's arm and forearm are bared and rest on a table at a comfortable height and in a good light. With a pen put a row of ink marks about 5·0 centimetres (two inches) apart down the arm and forearm. The scalpel should be carefully washed and dried on a clean towel. No trace of antiseptic should remain on the blade, as this is very liable to produce "pseudo-reactions". With a finger and the thumb of the left hand stretch the skin taut in the region of the first ink mark and make a light stroke with the scalpel about a centimetre from the mark. The cut should be only deep enough to show the pink tops of the papillæ and should not cause bleeding. Put a cut similarly beside the other ink marks and then examine each again to see that it is deep enough by stretching the

skin. In doing tests avoid deeply tanned areas, as these do not react well. Hairy areas should also be avoided. The skin near the flexure of the elbow is unduly irritable and should not be used. Liquid test reagents are applied with the looped applicators. The skin in the region is stretched so that the cut is held open and the reagent is rubbed in gently but thoroughly. When using powdered reagents, such as pollen, put a drop of solvent on the cut and then with a spatula apply some of the powder and mix it into a paste and rub well in, stretching the cut open with the finger and thumb of the left hand. The most useful solvent is Cocas buffered saline solution, but N/100 sodium hydroxide solution is quite satisfactory. For rough tests a saltspoonful of washing soda in a cupful of warm water is near enough. If a patient is sensitive to one of the reagents, he usually notices itching near the scratch, and within a minute or two a pink flush appears and spreads, and within about ten minutes a white wheal appears and grows irregularly. Within about twenty minutes its edges become less clearly defined, and in an hour or so it usually disappears. A reaction is regarded as positive only if most of the other tests in the region remain quiescent. It is always wise also to retest after an interval of a few days to make sure that the reaction is a real one.

Intradermal Tests.

Intradermal tests should never be done until it is quite certain that the reagent to be used does not react strongly when applied to a scratch. Numerous instances are on record of dangerous and even fatal "constitutional" reactions occurring after intradermal injection of comparatively minute doses of some reagent to which the patient was unusually sensitive. For instance, Cooke has reported death within a few minutes in a boy after intradermal injection of 0·1 cubic centimetre of a solution of fish glue, in spite of energetic treatment with adrenaline and other antidotes. For these tests Jena glass "tuberculin" syringes fitted with very fine, sharp needles are most convenient. These should be sterilized by boiling.

About 0·1 cubic centimetre of sterile buffered saline solution is first injected intradermally as a control; then small quantities of sterile extracts of the reagents are injected intradermally. About 0·01 cubic centimetre is usually sufficient, and this quantity forms a wheal about the size of a pin's head if correctly injected. Care should be taken not to have bubbles in the syringe, as any air gives rise to "pseudo-positive" reactions. Care must also be taken that no iodine or spirit adheres to the outside of the needle. Reagents are usually sucked out of rubber-capped bottles similar to those used for insulin. When iodine is used in sterilizing the tops of these, it should be allowed to evaporate before inserting the needle, and when the syringe is charged a drop of reagent should be allowed to flow down the needle to wash it before the injection is made. These tests are observed for about ten

to thirty minutes. As a rule it is not necessary to test pollens in this way, as sufficiently definite reactions are produced by the scratch test if dry powdered pollens are used; but certain test reagents which are known to be rather weak reactors should always be tried in this way before deciding that they are unimportant. Especially is this true of "house dust", feathers and kapok.

Modifying Factors.

A large dose of adrenaline will temporarily lessen the size of reactions or prevent them completely. Possibly ephedrine may have a similar effect.

Sensitiveness to a food may disappear for some weeks after severe urticaria caused by its ingestion.

Febrile conditions and some exanthemata will cause temporary disappearance of reactivity, and it is interesting to note that a patient who reacts definitely to the von Pirquet tuberculin test is said to lose his reactivity sometimes for months after measles. Rapidly developing tuberculosis seems sometimes to give rise to dermographia, but it also frequently enhances preexisting allergic conditions.

Recording Results.

Positive reactions in the scratch test occur within about ten minutes, but the test should be observed at intervals for at least thirty minutes, as some individuals react very slowly. In rare cases reactions may occur only after one or two hours or longer, but probably these are sufficiently uncommon to be ignored.

After the reagents have been in contact with the scratches for about ten minutes, wash them off with cotton wool swabs dipped in warm water. Of course a separate swab must be used for washing each scratch and another dry swab used for drying the area. After reading the reactions dab each scratch with iodine or spirit.

As a rule, if the tests are well done, there is no difficulty in deciding which tests give positive results. If undue trauma has occurred, all the "scratches" will be surrounded with a flush and slight wheal, even if no reagent is applied, but with very little practice it will be possible to insure that no reaction occurs round any of the cuts. The smallest positive reaction shows a tiny, raised, white, oval wheal surrounding the edges of the cut, with a pink flush extending perhaps for one centimetre round this. As a rule itching is noticed. This is recorded as a one *plus* (+) reaction. When the urticarial wheal is two centimetres or more across, with irregular outline and marked flushing of the surrounding skin, one records it as a three *plus* (++) reaction. Reactions intermediate between this and the smallest reaction are recorded as two *plus* (++) .

When observing intradermal tests the "control" injection of buffered saline solution should be closely inspected. In most cases it will have practically disappeared in ten or fifteen minutes, but in perhaps one-fifth of all cases tested a lump about 0·5 centi-

metre across will have appeared, usually not surrounded by flushing. One would then regard as positive only those results of intradermal tests showing a lump at least twice as large as the control, and one would be sceptical of their significance unless: (a) the outline were irregular, with small pseudopodia, (b) there were surrounding erythema, and (c) itching were noticed.

Other cases give good negative results with control injections of saline solution, but give small symmetrical lumps wherever any protein extract has been injected. There is no surrounding flush or itching, and one can usually decide that there is no reaction.

In spite of these atypical reactions, in most cases the test is simple to perform and gives clear-cut results. But one would repeat the warning that it must on no account be used until scratch tests with the reagent in question have been found to produce no reaction.

THE VALUE OF NUX VOMICA TREATMENT.

By FELIX ARDEN, M.D. (Adelaide),
Adelaide.

No other apology for writing about so familiar a substance as *Nux Vomica* is needed than to say that it was condemned recently by a colleague of mine as "the most useless drug in the Pharmacopœia". And this remark, scathing as it may seem to large numbers of practising physicians, only echoes the opinion held in Germany at the beginning of the present century, and probably still held.

"I was rather astonished", wrote Lauder Brunton in 1901, "to find in a German book on pharmacology and therapeutics, the statement that strychnine is of no use at all; that it might just as well be expunged from the *Materia Medica*. This is very curious, inasmuch as it has been found by comparison with other prescriptions that strychnine, in the form of *nux vomica*, is more used than any other drug whatever in this country."⁽¹⁾

These two quotations emphasize the difference of opinion that exists about the therapeutic value of the drug. And it was with a view to solving the problem that I undertook the experiments here described.

Nux Vomica was known in Europe in the fifteenth century, but at first it was used only to poison noxious animals. There is no mention of it in the 1787 edition of the "Pharmacopœia of the Royal College of Physicians of London", but in the "Edinburgh New Dispensatory" (1786) the following paragraph appears:

Nux Vomica is the seed of the *Strychnos nux-vomica* (Lin.), a tree growing in the East Indies, where it is said to be used as a specific against the bite of a particular species of water-snake. It is considerably bitter and deleterious; but has been used in doses from five to ten grains twice a day or so, in intermittents, particularly obstinate quartans, and in contagious dysentery.

When we consider that the official dose of the seeds, adjusted to contain not more than 1·25% of strychnine, is only 0·065 to 0·26 grammes (one to four grains), we feel some respect for our hardy ancestors, who could take "five to ten grains twice a day or so".

Strychnine was isolated from *Nux Vomica* by Pelletier in 1818 and was first investigated by Magendie, who discovered its effect upon the spinal cord. Physicians began to employ it in the treatment of paralysis and found that "even when it did not cure the paralysis it tended to act as a tonic and strengthened people generally" (Brunton).

During the nineteenth century the drug became very popular, being prescribed for its general effect even in such states as tuberculosis, *diabetes mellitus*, Addison's disease and infantile paralysis.⁽²⁾

The pharmacological action of *Nux Vomica* is four-fold:⁽³⁾ (i) It increases the irritability of the cord and medullary centres and in large doses causes convulsions. (ii) It increases the acuity of the special senses. (iii) It has a slight action on the cerebrum and higher centres similar to that of caffeine, but much less pronounced. (iv) It is supposed to have some effect upon skeletal muscle, either by direct action or by way of the nerve endings.

The action upon the spinal cord is by far the most important, and can be proved by an experiment of Pousson to be due to sensitization and not to direct stimulation. A frog is dipped in a solution of cocaine until the whole skin is anaesthetized, after which it is found that strychnine will not cause convulsions because there are no incoming stimuli to the cord. If a sensory nerve is then exposed and stimulated, convulsions result.

Apart from cases of poisoning by substances which paralyse the anterior horn cells of the spinal cord or depress the respiratory centre, there is no morbid condition for which *Nux Vomica* is specific. But physicians use it generally with one of two objects: either to produce reflex stimulation, as in respiratory failure, or to combat over a long period such indefinite symptoms as loss of appetite, weakness and fatigue.

This paper is concerned only with the use of the tincture of *Nux Vomica* in the treatment of the latter type of case. Numbers of such people are to be found in the medical clinics of the out-patient department and in general practice. They feel unwell in a vague sort of way, but cannot describe their sensations; they harbour no obvious foci of infection and present no abnormal physical signs. They are not ill enough to be in bed, not well enough to be discharged, and drift along indefinitely. They are the bugbear of the out-patient physician.

A few months ago I set aside seventy-six outpatients of this type for observation and treatment. Each one was given *Tinctura Nuci Vomicae* in doses of 0·45 cubic centimetre to 0·6 cubic centimetre (seven and a half to ten minims), according to weight, made up to a drachm with *Aqua Chloroformi*, to be taken thrice daily in water before meals. All other drugs were discontinued in order to avoid

confusion. On their next visit the patients were encouraged to say what they thought of "the bitter medicine". Some of them may have attributed more benefit to it than was truthful in order to please me, but I do not think this happened very often.

Results of Treatment.

The patients after treatment naturally fell into four categories: (i) relieved (these patients said that the medicine made them feel better); (ii) unrelieved; (iii) made worse; (iv) did not return. The majority of the patients in the last category can be regarded as cured—at least temporarily. At any rate, they must have felt able to forgo their visit to the doctor. Many of them had been habitual attendants at the out-patient department. There was no other hospital to which they could have gone; and, to my knowledge, none of them died.

The classification of seventy-six cases of ill-defined disease presented some difficulty. Nine of the patients seemed to have an organic basis for their complaint and have been considered separately. The remaining sixty-seven were finally arranged as follows:

(a) Debility	30 cases
(b) Neurasthenia	18 cases
(c) Functional dyspepsia	8 cases
(d) Anxiety neurosis	6 cases
(e) Miscellaneous	5 cases

Admittedly the boundary-line between these various functional states is not well defined, but for the purpose of this experiment it is unimportant. All the patients had this in common: they felt in need of medical assistance, and complete examination failed to reveal organic disease. In the series there were forty-eight women and twenty-nine men, and their ages ranged from thirteen to sixty-five years.

(a) *Debility*.—The thirty patients whose condition was labelled "debility" for want of a better name, complained chiefly of physical weakness and fatigue, loss of appetite and loss of energy, which was in some cases the result of an operation or an illness, repeated pregnancies or overwork. After taking *Nux Vomica* sixteen felt better, the condition of two remained unaltered, and twelve did not return. The following are illustrative cases:

CASE I.—A.W., aged thirty-one years, complained that he had been losing weight for several months and was very weak and tired. He had a slight cough, was unemployed and introspective. Examination and an X ray picture of his chest revealed no abnormality. The systolic blood pressure was 130 and the diastolic 65 millimetres of mercury. The patient's condition did not improve on administration of bromides; he said that he felt weak and could not eat. He was given 0·6 cubic centimetre (ten minim) doses of *Nux Vomica*, and after a fortnight said that this "had done him more good than any medicine he had ever had".

CASE II.—T.F., a labourer, aged sixty years, complained of pains in his chest and stomach, weakness, and a general feeling of ill-health; he vomited occasionally. There was no evidence of carcinoma. After taking 0·6 cubic centimetre (ten minim) doses of *Nux Vomica* for three weeks he reported that he had "improved seventy-five per cent." His medicine was repeated, and I did not see him again for five months, after which he returned suffering from a relapse.

CASE III.—A.C., aged forty-nine years, a housewife, had been "growing tired and weak for nine months". Her legs could hardly carry her; she suffered from backache; walking short distances made her breathless. Except for obesity there was no abnormality found on examination. She was given 0·6 cubic centimetre (ten minim) doses and reported after a fortnight that she felt slightly better, but not much. She continued to take *Nux Vomica*, and after another fortnight said that she was better and able to do more work.

CASE IV.—M.C., a married woman, aged sixty-four years, complained of feeling weak after an attack of influenza. She was given 0·6 cubic centimetre (ten minim) doses and returned in four weeks to say that the medicine had done her a lot of good. It was repeated and she did not return.

CASE V.—M.L., aged thirty-years, had been attending the out-patient department for a long time, complaining of general ill-health. She was underweight, had no appetite, and felt weak. There were no physical signs of disease; an X ray picture of her chest revealed no abnormality, and her urine was free from cells. She was given 0·45 cubic centimetre (seven and a half minim) doses and did not return, although she had been coming monthly to the hospital for over a year.

CASE VI.—S.M., a market gardener, aged forty-six years, suffered from general weakness and loss of weight and was easily exhausted. Examination revealed no abnormality. He was given *Nux Vomica* in 0·6 cubic centimetre (ten minim) doses and did not return.

(b) *Neurasthenia*: "A condition of weakness or exhaustion of the nervous system, giving rise to various forms of mental and bodily inefficiency" (Osler).—There were eighteen such patients in my series. Four derived benefit from *Nux Vomica*, in five the condition was unchanged, one was made worse, and eight did not return.

CASE VII.—E.F., a widow of forty-one years, had been ill since her husband was killed eighteen months before. She suffered from pains in her stomach with acid eructations and vomiting, shortness of breath on exertion, headaches, giddiness, and black specks before her eyes. Examination revealed no abnormality. As the patient's condition did not improve after two months on bromides, I gave her 0·45 cubic centimetre (seven and a half minim) doses of *Nux Vomica*, which seemed to suit her. She came up on four occasions to say that she was better, and was still on *Nux Vomica* at the end of the observation period.

CASE VIII.—M.F., aged forty years, had been attending the out-patient department for about twelve months, complaining of attacks of headache and shaking, and feeling as though she were about to die. She had also a sensation of fullness in the throat and pains in the elbows, hands and knees. No abnormal signs were discovered. She was given 0·45 cubic centimetre (seven and a half minim) doses of *Nux Vomica* and came back in four weeks for more, saying that she felt better. Her medicine was repeated and she did not return.

CASE IX.—K.R., aged forty-three years, had been attending the out-patient department for eighteen months. He dated his symptoms from the War, saying that his nerves were bad, he could not sleep, had lost all energy for work, could not concentrate, and had pains in his limbs. In appearance he was a prematurely aged man, thin, anxious and tremulous. Examination otherwise revealed no abnormality. He was given 0·6 cubic centimetre (ten minim) doses of *Nux Vomica* and did not return.

CASE X.—G.F., aged forty-five years, complained of his "nerves". He felt shaky at times and had strange feelings in his stomach and head, and attributed his symptoms to the loss of all of his six children. Nothing abnormal was found on examination and the Wassermann test yielded no reaction. He was given *Mistura Gentianæ Acida* on

three occasions without relief. Afterwards he was put on to *Nux Vomica* in 0·6 cubic centimetre (ten minim) doses and did not return.

(c) *Functional Dyspepsia*.—Eight patients in this series suffered from indigestion. Two elderly women complained chiefly of flatulence; one man suffered from visceroptosis; and another complained of "a sick feeling in the stomach and giddiness". No patient showed any evidence of cholecystitis, peptic ulcer or neoplasm. The condition of three of these people improved while they were taking *Nux Vomica*; two were unrelieved and two did not return. One young man with hyperchlorhydria was made worse.

CASE XI.—C.D., a married woman of sixty years, had been suffering from flatulence for twelve months. She had attacks of belching at night and "a sour taste coming up from the stomach". Radiological examination after administration of an opaque meal revealed no abnormality. The patient was given 0·45 cubic centimetre (seven and a half minim) doses of *Nux Vomica*, and she said that it did her good.

CASE XII.—J.F., aged twenty-four years, had been attending the out-patient department fortnightly for the past six months, complaining of discomfort after meals, epigastric fullness and loss of appetite. Examination after a test meal revealed a low acid curve, but the patient did not lose his symptoms when taking *Acidum Hydrochloricum Dilutum*. He was given 0·6 cubic centimetre (ten minim) doses of *Nux Vomica* and was still taking it at the end of the observation period, after coming up on three occasions to say that he felt better.

(d) *Anxiety Neurosis*.—Six of the patients in this series suffered from some form of mental conflict, which expressed itself by tremors, fainting attacks, phobias of various sorts, depression and insomnia. After treatment with *Nux Vomica* three of these patients felt better, two were unrelieved and one did not return.

CASE XIII.—G.L., aged thirty-five years, felt unable to do her work. She was losing weight, slept badly, and her hands used to sweat. Her husband had deserted her ten months previously. The patient was thin, but otherwise normal on examination. She was given *Nux Vomica* in 0·45 cubic centimetre (seven and a half minim) doses for a month, after which she had "improved in every way", was sleeping well and wanted to return to work.

(e) *Miscellaneous*.—Three patients with hysteria were not relieved by *Nux Vomica*. One was a boy of seventeen who had hysterical fits; the second, a woman who had just recovered from an hysterical paresis of the right leg and complained of "fainting attacks"; the third, a man with traumatic hysteria following an accident.

One patient, who complained of pains all over the body, loss of energy and despondency, was made worse. He was a hypochondriac, and with some excuse for it, his previous illnesses being tuberculous hip disease at the age of twenty years, lead poisoning at thirty-five, ruptured gastric ulcer followed by subphrenic abscess at fifty-eight, pneumonia at sixty-one, and several minor complaints.

Lastly, a woman of forty-four, suffering from menopausal symptoms after a panhysterectomy, complained that she "went funny all over after taking the medicine".

Table Showing Results of Treatment in Functional Disorders.

Clinical Condition.	Relieved.	Unrelieved.	Worse.	Did Not Return.
Debility	16 cases	3 cases	—	12 cases
Neurasthenia	4 cases	5 cases	1 case	8 cases
Functional Dyspepsia	3 cases	2 cases	1 case	2 cases
Anxiety State	3 cases	2 cases	—	1 case
Miscellaneous	—	3 cases	2 cases	—
Total (67 cases)	26 cases	14 cases	4 cases	23 cases

Organic Disease.—In the group of nine cases in which there was some organic disease present, *Nux Vomica* was exhibited in the hope of relieving the weakness and weariness which formed these patients' chief complaint. But the experiment was unsatisfactory. Three sufferers from hyperpiesia were made worse, and in one only was the condition improved; cases of fibrosis, peripheral neuritis and chronic cervicitis were unrelieved; and an elderly man with obesity and myocardial insufficiency was made worse.

Functional Disorders.—The above table shows that a fair proportion of the sixty-seven patients suffering from functional disorders obtained relief from *Nux Vomica*.

It is not necessary to use the drug by itself, as I have done. In many cases the combination of *Nux Vomica* with potassium bromide is more effective than either of these substances alone.

Conclusion.

The purpose of this investigation was to ascertain whether *Nux Vomica* was of value in therapeutics. Having completed it, I feel that the nineteenth century English physicians were right and that the Germans and my cynical colleague were wrong. For it seems that in *Nux Vomica* we have a remedy for "debility" and similar indefinite states, a remedy which is simple and frequently successful and always worthy of a trial.

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THE STUDY OF EARLY INFANCY: A PLEA FOR COOPERATION BETWEEN THE SCIENCES OF MEDICINE, PSYCHOLOGY AND EDUCATION.¹

By P. MOLITOR BACHELARD, Ph.D.
Lecturer in Experimental Education and Educational Psychology, University of Melbourne.

IT has been said that the child is father to the man. Character development may be likened to the

formation of a statue by the pouring of metal into a mould. Native endowment, intellectual and emotional, is the precious metal; it is precious because no human ability can be considered valueless. That which moulds a child's inborn powers of thinking, feeling and willing is mainly the environment into which the accident of birth has thrown him. The more one studies the development of man from birth to full manhood or womanhood, the more it becomes evident that these environmental influences require not many but only a few years to fix the fundamental type of character that will mark the child throughout life with an individuality all its own. Preyer, an eminent student of early childhood, writes:

Man in the first three years of life accomplishes a mental development which, in range and extent, is scarcely less than the development of the whole of his after-life.

The character of the child will develop with the years: it may become refined or uncouth, high or low, broad or narrow, deep or shallow, but the pattern determining the lines of development has been laid down in the early years of life under the moulding influences of home, parents, relatives and companions. Many feel averse to admit that human personality is determined in all its outlines by the factors of endowment and environment as inevitably as the physical build of a continent is determined by geological and climatic conditions. Yet all must admit that in a man's life his past forms a mental pattern which, to a larger extent than is generally recognized, shapes that man's present behaviour. If we could gain a clear idea of a child's inborn capacities and of the characteristic mould into which his intellectual and emotional endowment has been fashioned by the first two or three years of his life, we should be able to predict what kind of man or woman that child would be. There is no doubt then that an accurate knowledge of child nature is of the utmost importance for parents, physicians, psychologists and educators. Yet little has been done to further scientific studies of early childhood.

We recognize the importance of studying the nature and satisfying the educational needs of children at school age. At this later stage of development all civilized countries supply a free education to all children. In his tender years, when most responsive to the influences surrounding him, the infant is left to the loving but often unenlightened care of parents. These years, fundamental for future

¹ Read at a meeting of the Australian and New Zealand Association for the Advancement of Science, Melbourne, January, 1935.

development, should be specially studied and provided for, not necessarily by establishing community crèches and nurseries, but at least by giving help to parents in their difficult task. What do we find? Splendid work is being done in regard to the physical growth of the child in hospitals and baby welfare centres. It is but right that we should begin with the physical aspect of development, since physical health is the more obvious need of the child and the first requisite for mental health. In human welfare, however, it is the mind that counts even more than the body. On the physical side much scientific work has been done regarding the normal weight and height for each age, the causes of sickness and their remedies, the kind of food, clothing *et cetera*. Little has been done to establish age-norms for intellectual development. Apart from some one-sided psycho-analytical attempts, there is hardly any study existent to trace the many causes of emotional disturbances that may occur in early infancy. We know next to nothing about the means of detecting and remedying by special treatment, educational or otherwise, backwardness in mental development which may manifest itself in early life.

The great educationists of the past (Comenius, Rousseau, Pestalozzi and others), apart from wonderful intuitions regarding child nature, have contributed little towards an experimental and scientific study of the subject. For several centuries educationists have recognized the necessity of building education on the principles of psychology, but the psychology they had in mind was a general psychology of the Herbartian type, a logical analysis of mental activities as they occur in adults or, rather, in the individual psychologist himself. It is mainly the medical profession that comes in contact with babies, and we owe to the physicians the first attempts at an objective study of mental powers as they gradually unfold themselves in the first years of childhood. The contributions of experimental psychologists came later. All these are isolated studies, diaries describing the physical and mental growth of the writers' own children. In recent years more systematic studies of groups of children have been attempted by the establishment of child study stations connected with universities, for example at Iowa and Yale. This movement of child study must have a beneficial effect on public welfare. It is the first and most necessary step of the mental hygiene movement for a mentally healthier generation. Prevention and early correction are preferable to cure at a later stage. These studies hold out neither promise nor threat of making every baby a perfectly normal, in the sense of standardized, adult. The purpose is precisely to recognize individual differences and to help individuals to make the best of these characteristics. In particular, investigations of this kind will raise the value of baby welfare centres, nursery schools and kindergartens and will appreciably help the community in tackling the ever-present problems of mental deficiency and juvenile delinquency.

Baby Welfare Centres.

Baby welfare centres will be given scope for wider activities. Investigations of mental development from early years will enable us to pick out the more outstanding items of behaviour which are symptomatic of growth. The establishment of mental norms will give to all concerned with the welfare of babies, and therefore of the community, valuable, if not infallible, instruments for detecting normal, accelerated and retarded growth, and for remedying, at as early an age as possible, defects in mental development. If we possessed norms of mental growth in infancy that are reliable and easy of application, nurses in baby welfare centres could use them with the same facility as they use norms of physical growth. They could advise parents in the matter not only of physical, but also of mental health, which generally is allowed to take care of itself till the child reaches school age. Then it is often too late. Neglect of a child with a subnormal rate of bodily growth may prove fatal as regards physical health. May not neglect of intellectual and emotional growth in the first plastic years of life prove equally fatal as regards mental health? The supervision of food for the baby is considered all important. In practice the community at large attaches little importance to the proper supply and regulation of mental nutrition and stimulation in the early years of life, when mental attitudes begin to set and form the basic and most unchangeable patterns of behaviour in adult life. Reasonable success in an investigation of this kind, then, will open up new possibilities for baby welfare centres. Already doing such efficient work, they may yet double their usefulness by becoming real life cells in the community, promoting the mental as well as the physical health of coming generations. Of necessity these norms will at first be but rough, although serviceable, measures for diagnosing mental growth and suggesting the advisability of special attention. The wide use of them in baby welfare centres and by medical practitioners and progressive parents will in time supply sufficient data to increase their reliability. Once we have a large number of babies whose mental development has been recorded, it will be an easy matter to make follow-up studies in nursery schools, kindergartens and the first years at elementary schools. These studies must inevitably show which mental manifestations at an early stage of life are, on an average, significant indications of those rates of intellectual and affective-conative growth, whether normal, accelerated or retarded, that must be considered relatively permanent.

Diagnosis of Mental Defect.

This will mean a great advance in the treatment of mental deficiency. If we had means of discovering at an early age those children who are characterized by such retardation, that the probability of scholastic, economic and moral adaptation to their environment is of the slightest, two important results would follow. The first would be that

medical and psychological science would be given opportunities for studying these defects in their early manifestations and possibly devising remedial treatment. Secondly, educators would be enabled to differentiate school methods from the very beginning to suit the method of teaching to the needs and capacities of each child. As things are now, medicine, psychology and education are first faced and baffled by the seeming incurability of mental deficiency when it manifests itself at school age and can no longer be ignored. Teachers must wait till a child has been at school for about two years before they feel certain that it is a case of inherent mental backwardness. The specialized instruction then given to these children will suffer from the great disadvantage of having been too long postponed. When education became compulsory for all children the fact that there are great and permanent individual differences in rate of mental development soon forced itself upon the attention of educators. We consider normal those children who in a year advance one step on standardized mental scales, such as Binet's. That step is conceived as one mental year. There is a fair number of children who yearly advance by more than one mental year, and there are just as many who advance by less than one mental year. This is the class of retarded children. Some we know as idiots, their mental development being so slow that the best of them, when adults, do not proceed beyond the mental level of three-year-old children. Imbeciles remain below level six, and few feeble-minded adults score a mental age as high as ten years. In a survey of Victorian special schools, made in 1933, the average mental level is that of ordinary children at the age of six and a half. Their average physical age is eleven. Their average mental retardation amounts to three and a half years. The ratio between their physical and mental ages works out at 0·6. Psychological research has proved that this quotient generally remains fairly constant and that in the case of retarded children it tends to a slight decrease with increase of age. Therefore we may say that the yearly mental advance of these children is little more than one-half of the rate of growth of ordinary children. The typical child of this group is one whose mental growth at the age of sixteen does not extend beyond the level of normal children eight years old. An examination of the mental levels for the separate ages of these same children, from age six and a half to fourteen and a half, gives the same results.

Physical age: 6·5 7·5 8·5 9·5 10·5 11·5 12·5 13·4 14·5
Mental age: 3·3 4·7 5·8 5·5 6·1 7·3 7·4 7·9 7·9

Over a range of eight years there is an increase of mental capacity from 3·3 to 7·9. This means a yearly rate of 0·57. Therefore the rate of mental growth of these children is roughly only one-half of a year of normal progress. That these figures are not mere statistical accidents is shown by the fact that the results obtained by Professor Burt from his investigation of the special schools in

London are in close agreement with our figures. It is most probable that the permanent differences in rate of growth which are observed in children of school age, manifest themselves in outward and measurable behaviour from the tenderest years. This assumption seems fully justified at least in the case of retardation as a group, although exceptions may occur. What, then, is urgently required is reliable means for at least signalling danger of permanent mental retardation at an early age.

Such early diagnosis will materially enhance the prospects of medical science in finding effective remedies. Inherent mental deficiency is generally considered incurable, but incurability is a relative term. We may consider the mind and body as but two aspects of the same ultimate reality, or we may be persuaded that the mind is something apart from the material organism. Yet even those who favour the latter opinion will accept that mental activities are conditioned by organic activities and that an inherent defect in mental activities may be remedied by a change in its corresponding organic conditions. In either opinion there is held forth promise of success for medical research. Not so long ago the dwarfish mental and physical stature of cretins was an incurable defect. It is a great achievement of the medical profession to have traced this condition to thyreoid deficiency. Given greater opportunities for research into deficiency diagnosed at an earlier stage, there is no reason why this achievement should not be repeated, even in cases which up to now have generally been considered as belonging to the class of inherent primary and incurable amentia. There is even greater hope that with early diagnosis abnormal temperamental inadequacies may be mitigated by research into endocrine disturbances.

In discussing differences in mental ability it is preferable to speak of mental development than of innate capacity. The latter concept may lead to the pessimistic view that native endowment is the only factor in determining actual growth. We may, with as much justification, explain the individual differences in size of oaks on the ground that these differences are due to different inborn capacities for growth of individual acorns, considered as forces largely independent of conditions of soil and climate. In the light of our present knowledge of the interdependence of nervous and mental activities it seems hardly permissible to conceive the mind as having an innate capacity for growth all its own and independent of the growth of the nervous system. In such an opinion the immaterial something we call the mind could have no point of contact for the material ministrations of medicine. But if we consider, as we must, that mental growth and nervous growth are strictly correlative terms, there is no assignable *a priori* reason why mental growth may not be intensified by direct treatment and exercise. Indeed there is every reason for belief that further medical research will lead to a revolutionary treatment of mental defects.

Education of Defectives.

Meanwhile much work must be done for the education of mental defectives. The number of intellectually and temperamentally subnormal children will not be materially reduced in the near future. Legal means for controlling marriage, either by sterilization or segregation, will not in a short time bring about an appreciable diminution of mental defect in the community. Many families, because of their religious persuasion, will refuse to avail themselves of this legal opportunity. Even if all were ready to accept this control, the aim of the law would not be attained for a long time. The carriers of mental defect are, beside the class of certifiable feeble-minded, imbeciles and idiots, the much larger class of less retarded and non-certifiable persons, which constitutes at least 10% of the community. The most opinionated eugenist will not dare to advocate surgical operation on such a vast scale. To rid Australia of Alsatian dogs one can employ simple means, stopping importation and either killing them all or preventing propagation. They form a class apart; the mental defectives do not. The community will continue to be faced by this perplexing problem of intellectual and emotional subnormality of many of its members.

It is objected that it is waste to spend on defectives good money and valuable human energy, which would better be spent on raising the efficiency of the better endowed. This objection would hold if it were within the bounds of possibility for modern communities to revert to the Spartan custom of killing all the unfit at birth. Setting aside the opinion that physical, intellectual and economic efficiency should be the only aim of progressive states and that the devoted care given to the weaker members has not a moral and ennobling effect on the whole community, we cannot deny that in the long run it is cheaper to educate defective children to become contented, law-abiding and to some extent self-supporting citizens than to allow them to drift till they reach adult age and then to pay enormous sums for their support or incarceration.

In the education of this large number of more or less retarded children an early diagnosis is required to enable psychologists and educators to devise and supply from the beginning an educational environment that in most cases will minimize the deficiency and in many cases will remove the obstacles in the way of fairly normal development.

Conclusion.

In conclusion it may be said that it will mean progress for the physical, intellectual and moral well-being of the community if, by the concerted action of medicine, psychology and education, means are devised for diagnosing, curing or minimizing mental deficiency at an early stage of development. At the same time early mental diagnosis will make it possible to cultivate many superior talents that in mass education are in danger of remaining hidden and unheeded.

It is unlikely that some fairy hand will pour sufficient golden coins from its horn of plenty into the coffers of our universities for the establishment of psycho-clinics. Is it too much to hope for coordinated action of physicians and nurses, psychologists and educationists in investigating human development from its early beginning? The importance of the problem cannot be overlooked. A. Gesell, the Director of the Yale Psycho-Clinic, writes:

The infant embodies life while it is in the most sensitive, the most responsive phase of the cycle of growth. He holds Promethean sources of life.

Reports of Cases.**A CASE OF HÄMOGLOBINURIA COMPLICATING PULMONARY TUBERCULOSIS DURING THE ADMINISTRATION OF GOLD.**

By DAVID B. ROSENTHAL, M.D., B.S. (Melbourne),
M.R.C.P. (London),
*Medical Superintendent, Gresswell Sanatorium,
Mont Park, Victoria.*

Koch, in 1890, noted that gold salts had a bactericidal effect on tubercle bacilli *in vitro*.

Ten years have elapsed since preparations of gold were definitely introduced into the treatment of pulmonary tuberculosis, but the utility of this treatment is still not established. At the same time the limitations of application are defined both by the suitability or otherwise of each individual case and the risk of the occurrence of complications, the toxic effects experienced being those common to therapy with heavy metals and modified by the field of therapy. These complications have been well described and are set out by Burrell⁽¹⁾ and Morriston Davies⁽²⁾ thus: (i) febrile reactions, (ii) albuminuria, (iii) gastro-intestinal symptoms, mainly vomiting and diarrhoea, (iv) aching in limbs and joints, (v) erythematous rash.

Both writers comment on the importance of dosage of the gold salt in the production of these complications, and agree that when albuminuria occurs, in most of these cases the condition is mild and transient.

Amberson, McMahon and Pinner,⁽³⁾ reviewing twelve patients treated with "Sanocrysin", state: "All patients treated showed evidence of damage to the renal tubules."

Mansell,⁽⁴⁾ in respect of 153 cases of pulmonary tuberculosis treated with "Sanocrysin", reports albuminuria in as many as 27.5% of patients so treated. Cruden,⁽⁵⁾ recording the treatment of fifty cases of pulmonary tuberculosis by gold salts (various preparations), reports the occurrence of albuminuria in only 4% of cases and gives details of one case in which acute exfoliative dermatitis occurred, associated with profuse haematuria, which lasted for seven days.

Examination of the literature on the subject adds little to the above information. Most workers have used "Sanocrysin", but other preparations are now being administered more freely. In the case here recorded the patient was treated with intramuscular injections of "Solganal B" (containing about 50% gold), a preparation which has given rise to only few complications in my series.

Clinical Notes.

W.C.S., male, aged twenty-eight years, married, a labourer by occupation, was admitted to this sanatorium on April 16, 1934, suffering from pulmonary tuberculosis. The history of the case prior to this date suggested that

the infection had existed since 1930, when the patient was in bed for one week with "pleurisy". In October, 1931, a severe haemoptysis (one pint) occurred, and since then cough with sputum had persisted. More recently, the sputum was blood-stained, loss of energy and weight had been noticed, and night sweats were not infrequent. There is no temperature record of this period.

A possible source of infection was a brother, with whom he had shared a room and who had died of pulmonary tuberculosis in 1923. The patient admitted to taking "moderate beer".

At the time of his admission to hospital his general state was good. His physique was rather that of the plethoric type. He complained of dyspnoea on exertion only, and of cough with sputum.

Physical examination revealed in the lungs signs that suggested a bilateral chronic fibrocaceous type of infection, with a large cavity in the right subclavicular region, where there were a few crepitant rales.

In the heart no abnormality was present, other than irregular extrasystoles. The systolic blood pressure was 130 and the diastolic pressure 78 millimetres of mercury.

The abdomen and the central nervous system were both normal. Severe gingivitis was noted.

The specific gravity of the urine was 1010. Its reaction was alkaline; it contained phosphates, but no albumin and no sugar; microscopically it was clear.

On April 17, 1934, the sputum contained tubercle bacilli.

On April 18, 1934, the following report was made after radiological examination of the chest: "Heavy infiltration of fibrous type throughout both lungs, with the formation of many cavities. One particularly large cavity opposite the anterior end of the third rib, in the right lung. Trachea deviated markedly to the right."

On April 20, 1934, the blood sedimentation index was 26 millimetres (Cutler's technique).

The temperature chart showed daily variation from 36.9° C. (98.4° F.) in the morning to about 37.8° C. (100° F.) in the evening. The clinical picture was one of chronic fibrocaceous pulmonary tuberculosis with moderate activity.

In addition to routine sanatorium régime, it was decided to give a series of gold injections, the preparation used being "Solganal B", by intramuscular injection once a week. The initial dose was 0.001 grammes followed by 0.005 grammes, the dose being then doubled, as long as no reaction occurred. By the end of May the temperature had become steadier, averaging 37.2° to 37.3° C. (99° to 99.2° F.) in the evening, with general improvement corresponding. Early in July this improvement had been maintained and the weight had increased from 61.6 kilograms (nine stone eleven pounds) on admission to 65.7 kilograms (ten stone six pounds). The blood sedimentation index was now 22 millimetres. The temperature varied from about 36.7° C. (98° F.) in the morning to 37.2° C. (99° F.) in the evening.

On July 8, 1934, the temperature rose suddenly, reaching 39.2° C. (102.6° F.) at 8 a.m.; the patient then complained of pain around the left costal margin, pleural in type. Examination of the chest revealed moist sounds (as above) at the right apex; in addition there was a fine pleural friction rub at the base of the left lung and in the lower part of the left axilla. Symptomatic treatment was applied, the patient was put at rest, and a light fluid diet was given. Injections of gold had been given once a week, the previous injection being 0.1 gramme given intramuscularly five days previously. No further injections were given.

(It might be stated at this stage that the urine of all patients receiving gold injections is tested as a routine measure twice weekly during the course of injections.)

Urine tested on July 4, 1934, contained no albumin.

On the morning of July 11, 1934, a specimen of urine was left in the pathology department by the ward sister, who "thought it looked funny". And it did! The appearance was dark red, "smoky", so typically seen in acute scarlatinal nephritis.

On examination this specimen showed much macroscopic blood; the reaction was acid to litmus; the specific gravity was 1016. Microscopically it contained many red blood

corpuscles and pus cells, with a few granular and cellular casts. On examination of the centrifuged deposit with Gram's stain Gram-positive cocci were present; with the Ziehl-Neelsen stain no tubercle bacilli were seen.

The patient's general condition was fair, headache and thirst being the prominent symptoms. There was some dysuria, but no definite pain on or frequency of micturition. The systolic blood pressure was 116 and the diastolic pressure 70 millimetres of mercury. On general examination the condition appeared unchanged.

The progress over the next fortnight was one of gradual improvement; the temperature reached a maximum of 39.6° C. (103.4° F.) on the evening of July 12, 1934, and then fell by lysis, reaching 37.5° C. (99.6° F.) on July 22, 1934.

The pleuritic process in the left lung gradually subsided, a friction rub being audible for about four or five days. No signs of fluid appeared.

The quantity of urine passed was 600 to 900 cubic centimetres (twenty to thirty ounces) for the first few days, and then increased to normal, being 120 to 180 cubic centimetres (forty to sixty ounces) daily throughout the remainder of the patient's stay in the sanatorium.

On July 17, 1934, the blood sedimentation index was 33 millimetres.

The urine was examined daily, both for macroscopic appearance, by the guaiacum test for blood, and microscopically. A growing impression that the amount of red blood cells did not account for the quantity of blood pigment present was confirmed by careful examination of centrifuged specimen and by spectroscopic examination, which showed the presence of the absorption bands of oxyhaemoglobin, that is, the condition was one of haemoglobinuria.

Blood examined by the Wassermann test gave no reaction. On blood examination the erythrocytes numbered 4,300,000 per cubic millimetre; the leucocytes numbered 7,500 per cubic millimetre; the film was normal.

On July 19, 1934, the sputum was again positive for tubercle bacilli. The urine exhibited the same features as above; on examination with the Ziehl-Neelsen stain the centrifuged deposit was not found to contain tubercle bacilli.

On July 22, 1934, the urine definitely showed less coloration due to blood, and microscopically the deposit was much less. The diet was slightly increased.

On July 23, 1934, the blood urea was 76 milligrammes per 100 cubic centimetres.

The urine with the urea concentration test gave the following result:

(a) Pre-meal value	1.36%
(b) First hour after meal .. .	1.62%
(c) Second hour after meal ..	1.70%
(d) Third hour after meal ..	1.32%

On July 24, 1934, the general condition was improved. The patient complained of anorexia, but otherwise felt better. Micturition was normal. The systolic blood pressure was 114 and the diastolic pressure 80 millimetres of mercury. The ocular fundi were normal. In the chest no friction rub was audible.

The urine for the first time gave no reaction when tested with guaiacum; albumin was still present in a fairly large amount; the centrifuged deposit showed the presence of red blood corpuscles in small quantity and a few granular casts were seen.

On July 25, 1934, X ray examination of the renal tract revealed no abnormality.

On July 31, 1934, the appetite was good. The temperature varied from 36.4° C. (97.6° F.) in the morning to 37.5° C. (99.6° F.) in the evening. There were no urinary symptoms, but the urine still showed the presence of albumin and a few casts microscopically.

On August 21, 1934, the temperature was 36.8° C. (98.2° F.) in the morning and about 37.3° C. (99.2° F.) in the evening. The urine contained a trace of albumin in all specimens tested, and microscopically there were present a few casts, pus cells and red blood corpuscles. The blood urea was 35 milligrammes per 100 cubic centimetres.

The urea concentration test gave the following values:

- (a) Pre-meal value ... 1.34%
- (b) First hour after meal ... 1.38%
- (c) Second hour after meal ... 1.40%
- (d) Third hour after meal ... 1.59%

The systolic blood pressure was 114 and the diastolic pressure 72 millimetres of mercury.

On August 22, 1934, an X ray examination of the chest was made and the following report was made:

Right lung: Considerable improvement shown by absorption of exudate, generalized fibrosis and partial obliteration of cavity previously seen. Left lung: There appears to have been basal pleurisy with incomplete resolution, considerably diminishing the acuteness of the costo-phrenic angle, which is not, however, completely obliterated. The remainder of the lung shows changes somewhat similar to those seen on the right side. General condition is one of improvement.

Progress continued uneventfully until September 18, 1934, when a rather severe haemoptysis occurred, which was not, however, attended by a severe reaction, and no rise of temperature followed.

From now on further observation showed little change. The general condition of the patient was good, appetite was excellent and the weight increasing. There were no urinary symptoms, but the urine continually showed the presence of albumin with a few pus cells, red blood corpuscles and occasional casts.

On October 2, 1934, the blood sedimentation index was 25 millimetres. The patient was discharged on October 18, 1934, with still a trace of albuminuria. His weight was now 69.3 kilograms (eleven stone) that is, 7.65 kilograms (seventeen pounds) more than on admission. The temperature ranged from 36.4° C. (97.6° F.) to 37.2° C. (99° F.). The general condition was good.

Discussion.

Search of the literature has failed to reveal the report of a case of haemoglobinuria considered to be due to gold salts.

Haemoglobinuria is considered to be either paroxysmal or continuous, the former being due to either Raynaud's disease or syphilis, the latter to any hemolytic agent, such as potassium chloride, arseniuretted hydrogen or to an unidentified toxin.^(a) In this case there is no reason to suspect Raynaud's disease; and syphilis is considered unlikely by the absence of history or symptoms pointing to it, together with the absence of a Wassermann reaction.

What, then, was the "unidentifiable toxin"? It has been mentioned that the urine is tested as a routine measure throughout the course of the series of gold injections in all cases, the patients incidentally also being given glucose as a preventive of the skin complications frequently reported.

The urine of the patient was clear until at least four days before the onset of complications; the blood pressure was well within normal limits; ocular fundi were normal; and there was no sign of cardiac enlargement. There is no evidence therefore of any preexisting renal deficiency.

What quantity of gold had been administered? The dosage was as follows: 0.01 gramme, no reaction; 0.005 gramme, slight rise of temperature, quickly subsided; 0.005 gramme, slight rise of temperature thirty-six hours later, quickly subsided. Injection was omitted for one week. Then at weekly intervals 0.01 gramme, 0.01 gramme, 0.02 gramme, 0.05 gramme, 0.1 gramme, 0.1 gramme—no reactions after any of these, except the last, four days after which the rise of temperature occurred.

The total quantity of "Solganal B" given was thus 0.351 gramme, really a small amount, and less than one-tenth of that usually given in any series.

Another consideration is the possibility of tuberculous nephritis. Was there a latent tuberculous focus in the renal tissue which was activated by the injections of gold (that is, a focal reaction), just as apparently a focal reaction occurred in the lung at this time? Or was the complication a pure tuberculous manifestation, merely

coincident with the administration of gold. Haemoglobinuria, as distinct from haematuria, is not a recognized symptom of urinary tuberculosis.

Again, the absence of evidence of preexisting renal disease and the failure to observe tubercle bacilli in the centrifuged deposit from the urine also militate against this diagnosis.

It may be noted that from the time the acute manifestations of the complication had been revealed, development of the case was definitely in the direction of improvement, suggesting that the causal factor had ceased to operate. Of interest also is the absence of any of the other complications associated with gold therapy, although at times the patient had remarked on experiencing "rheumatic pains" in the limbs.

Summary.

1. A case of haemoglobinuria, occurring in a patient suffering from pulmonary tuberculosis during the course of a series of injections of a gold salt, is reported.

2. The absence of evidence of preexisting renal disease suggests that the gold salt may have been the agent responsible for the nephritis, coexisting with, or secondary to, the haemoglobinuria.

3. The possibility of tuberculous toxæmia being the causative factor is considered, although haemoglobinuria must be an exceedingly uncommon manifestation of this condition.

4. The necessity for careful observation, with routine urine examination of all patients with pulmonary tuberculosis receiving injections of gold salts, is emphasized.

Acknowledgements.

I wish to acknowledge my thanks to Dr. J. Bell Ferguson, State Director of Tuberculosis, for permission to publish the records of this case; to my assistant, Dr. H. M. L. Murray, D.P.H., for his careful pathological work in repeated examinations of the urine and for general assistance during the conduct of the case; and to Associate Professor Young, Physiology Department, Melbourne University, for kindly making a spectroscopic examination of the submitted specimen.

My gratitude is also due to the Medical Superintendent and the Pathologist of the Austin Hospital for Chronic Diseases, Heidelberg, for carrying out the blood urea and urea concentration estimations.

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Reviews.

PROGRESS IN NEUROLOGY.

DRS. W. RUSSELL BRAIN AND E. B. STRAUSS, of London, are the joint authors of a book entitled "Recent Advances in Neurology", now set out in its third edition.⁽¹⁾

As its title implies, the book consists of an exposition and consideration of important contributions to neurology made during recent years. The display is of necessity selective, because the contributions have been numerous and varied, but an effort has been made to confine choice to subjects having a clinical bearing, without neglecting pertinent aspects of physiology, pathology and treatment.

⁽¹⁾ "Recent Advances in Neurology", by W. R. Brain, M.A., D.M., F.R.C.P., and E. B. Strauss, M.A., D.M., M.R.C.P.; Third Edition; 1935. London: J. and A. Churchill. Demy 8vo., pp. 456, with illustrations. Price: 15s. net.

It happens that in this edition attention is specially drawn to developments concerning the neurotropic filterable viruses and what seem to be allied infections, so that several chapters are devoted to telling much that is new concerning epidemic encephalitis, herpes and infantile paralysis, as well as to explaining what is meant by the so-called acute disseminated encephalomyelitis occasionally associated with vaccination for smallpox, measles and other exanthemata.

In a short review it is impossible to name all the other subjects considered, but we may single out as worthy of special mention the chapters on intracranial tumours, extrapyramidal syndromes, the hypothalamus and various disorders of reflexes. We may add that throughout there is a striving "toward removing the sting from the criticism that the neurologist can diagnose but not treat".

The writers may at times trip when they tread fields of neurophysiology; in all other directions, however, their course is sure and steady. Also it is pleasing to find the dryness of an epitome watered and relieved by what two evidently experienced neurologists think of the matter. Moreover, the text is freely sprinkled with good illustrations, and at the end of each chapter a list of references is given so that a reader desirous of consulting original sources of information may do so.

To all interested in neurology we commend the publication as a reliable synopsis of current thought on the subject.

CONTRACEPTION, ABORTION AND STERILIZATION.

A VALUABLE account of the three great problems of contraception, abortion and sterilization is given by John Ellison, Aubrey Goodwin, Charles D. Read and L. Carnac Rivett in their work "Sex Ethics".

The sex problem of today is frankly and clearly discussed. The authors consider that efficient education on sex matters will do more to eradicate disease and illegitimacy than any religious or civil code. The physical expression of love is a natural act and any ideas of the sinfulness and mysteriousness of sex should be banished from the mind. Although this book is not intended primarily as a book on sex education, it contains much useful information on this subject.

The portion of the book dealing with contraception opens with a short history and is followed by a discussion of its legal aspects. It is interesting to read that the strictly legal position is, that according to common law it is illegal to prevent conception, although there is no doubt that the greater part of public opinion today condones and even commands the use of contraceptives in certain circumstances. The authors even envisage the day when contraception may be a right denied to none. The views of the various churches are described and will be helpful in the understanding of the development of many neuroses. Both the indications for, and the methods of contraception are clearly stated and there is much information that is not easy to obtain elsewhere and which medical men should possess if they are to give many of their patients the help they seek.

The legal and religious views on abortion are fully dealt with and there is a most useful chapter on the indications and the absolute contraindications for the induction of therapeutic abortion. This will be found invaluable by the young practitioner who above all needs clear instruction on this matter, as he will not have been very long in practice before some aspect of the problem will be presented to him. The methods of inducing therapeutic abortion and the usual method used in cases of criminal abortion are fully described with instructions for the guidance of the medical man who may be called upon to attend such a case.

The effect of conception control and sterilization as a means of developing a healthier race are probably over-

estimated by the authors, who do not agree in all respects with the opinion of the recent Departmental Committee as to the legal position of certain aspects of sterilization. It would appear to be advisable to be guided by the Departmental Committee, which stated that in the event of sterilization the consent of the patient would not be a good defence, even if he or she were capable of giving consent, and in the event of the patient's death it would seem that a charge of manslaughter might be laid against the operating surgeon. The indications for sterilization and the modern methods of carrying this out are described.

The book may be regarded as giving an authentic medical statement on subjects that are becoming increasingly important in modern medicine, and the majority of medical men would obtain much helpful information from it.

HYPNOTISM.

"HYPNOTISM IN THE TREATMENT OF DISEASE" is a small book of forty-four pages by Dr. B. Layton Lloyd.¹ The author does not intend the book as a treatise on hypnotism, but as a plan for its more extensive use.

There can be no doubt that hypnotism is a method of treatment that is practically neglected by the profession in this country and, further, there can be no doubt that there is no other method of treatment to compare with it in certain cases, such as simple insomnia, hysterical conditions, anxiety states *et cetera*. These conditions constitute a large proportion of the hospital out-patient population, and hypnotism is a means of treating these unfortunate people unsurpassed by, in fact it is greatly superior to, the constant drugging and drenching with salts and bromides that are the method of therapeutics employed to relieve the conditions above mentioned.

While we therefore agree with a good deal that Dr. Layton Lloyd writes, we think that the value of his book is considerably lessened by his dogmatic assertion such as occurs in the very opening sentence of Chapter I: "Hypnotism is the most powerful therapeutic agent known in the world today." It is rather difficult to continue to study the book after reading such a statement.

Dr. Layton Lloyd has a very high opinion of the possibilities of hypnotism as a therapeutic agent; he seems to be unaware that its possibilities are greatly limited by the fact that there are large numbers of people (probably some 50% to 60%) who cannot be hypnotized. A great number of psycho-neurotics are people of the obsessional or compulsionist type, and these as a rule cannot be influenced by hypnosis. In fact, it is a good rule to observe that if a person is hypnotizable, then his condition is not of the obsessional type. It is for this reason probably that some practitioners abandon treatment by hypnotism after having failed with it at their early trials. Treatment of sick people by hypnotism and suggestion requires considerable judgement and knowledge of the different character types of human beings. Success comes only by experience, but Dr. Layton Lloyd writes as if success can be obtained in practically every type of person and by any medical man.

The author gives an account of experiments which purport to demonstrate that by suggestion under hypnosis the known physiological effects of drugs such as morphine can be nullified, and he goes so far as to suggest as an inference from these experiments that under hypnosis a man might possibly be made immune to all vegetable and mineral poisons, also to insect bites and even to snake bites and poison darts. His alleged experiments would require confirmation by other workers before his conclusions could be accepted. The inferences he draws from his experiments are quite unwarranted, and the statement of such claims for hypnotism are likely to do much harm to the serious study of this subject. The author is far too dogmatic in his statements and the book is too loosely arranged to be useful.

¹ "Hypnotism in the Treatment of Disease: Its Scope: A Plea for Research", by B. L. Lloyd, M.B., D.P.H.; 1934. London: John Bale, Sons and Danielson. Crown 8vo, pp. 49. Price: 3s. 6d. net.

¹ "Sex Ethics: The Principles and Practice of Contraception, Abortion and Sterilization", by J. Ellison, B.A., M.B., B.Ch., F.R.C.S., F.C.O.G., A. Goodwin, M.D., B.S., F.R.C.S., C. D. Read, M.B., Ch.B., F.R.C.S., F.R.A.C.S., M.C.O.G., and L. C. Rivett, M.A., M.C., F.R.C.S., M.C.O.G.; 1934. London: Baillière, Tindall and Cox. Super royal 8vo, pp. 232, with illustrations. Price: 12s. 6d. net.

The Medical Journal of Australia

SATURDAY, MAY 4, 1935.

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FRACTURES.

THE treatment of fractures may be looked at from several points of view. The patient, generally a person who has to earn his living by his bodily exertions, is compelled to relinquish his work, sometimes for comparatively long periods. It is true that he is as a rule a worker within the meaning of a *Workers' Compensation Act* and will receive a certain monetary payment during the period of his disability. This payment may or may not be sufficient for the needs of himself and of those dependent on him. Nothing, however, can compensate him if he does not emerge from his period of treatment as sound of limb as he was before he met with his accident. The purely economic side of the question—the amount of money lost in wages and the amount of compensation paid unnecessarily—is another aspect to be considered. Hospitals have an interest in fracture treatment, for, with the exercise of skill and care, beds are not occupied for over-long periods and money is saved. Again, apart from his duty to his patient, the medical practitioner owes it to the science and art that he

practises, and to his own reputation, to secure good results in the treatment of fractures. A distorted and useless limb is a reproach to the art of surgery and may be a constant reminder to the medical attendant that he might have exercised more skill or taken more care in his treatment. It was probably considerations such as these that made the British Medical Association in England appoint a special committee "to consider the existing arrangements for the treatment of fractures and other associated injuries of the limbs and to make recommendations for possible improvement thereof". The report of this committee, published in the supplement of *The British Medical Journal* of February 16, 1935, is a document that should be studied by all medical practitioners who have to treat fractures or who have a voice in the control and management of hospitals.

The report, of course, deals with conditions in Great Britain, but much that it contains may be applied to Australia. Since every member of the Association receives *The British Medical Journal*, there is no need to give a summary of the report in this journal. Some of the statistics that are set out, however, call for special notice. A table is included in which are stated the average disability period in 276 cases occurring in adults not treated in organized clinics and the number of patients in this group who were permanently incapacitated. These patients are compared with patients of organized clinics. It was found that whereas incapacity remained permanently in only 1% of patients treated in organized clinics, in the series of 276 patients no less than 37% were permanently incapacitated. Further in this group the duration of disability was more than three times as long as it need have been. Small wonder is it that the main recommendation of the committee is that in all hospitals one surgeon should be placed in charge of the fractures; in other words, that fracture units should be formed. Four fundamental principles are stated: segregation, continuity of supervision, after-care, and unity of control. It is stated that in some hospitals in England a surgeon in charge of fractures has been appointed and has been paid on a part-time basis. The advisability of the

appointment of fracture units has been discussed on several occasions in this country. In large centres such a course could be easily adopted. But the wide country areas in Australia make it necessary that fracture treatment shall be undertaken by isolated practitioners; and many excellent results are obtained. Several parts of Australia have been divided into areas supplied by what are known as base hospitals. These hospitals should, in the interests of the patients and of the medical staffs, appoint one surgeon as fracture surgeon; and every other practitioner in the district should cooperate in making the department controlled by the fracture surgeon efficient and effective. An isolated practitioner who feels that he is not competent to treat a patient with a serious or extensive fracture can always put the injured limb on a suitable splint and have the patient transferred to a practitioner who has become known among his *confrères* as a fracture surgeon. He can do this without losing caste; and in any case it is surely better to transfer the patient to someone else than to have the deformity ever present in his small community as a monument of his inefficiency and as a constant reproach.

The British Medical Association Committee insists on continuity of supervision and after-care; sufficient emphasis has perhaps not been laid on the fact that the care of the patient should begin from the moment he meets with his accident. To this end ambulance units should be instructed in the use of the splints suitable for the particular fracture. The importance of this aspect was shown in a recent spirited discussion at a meeting of the New South Wales Branch of the British Medical Association. When a suitable splint has been properly applied, the limb should not be disturbed until the patient has been seen by the fracture surgeon, and then only on his express instructions, and preferably under his supervision. A final point is that after-care should be continued by the surgeon until the patient is fit to resume his occupation. The custom, still existing in some places, of discharging a patient from a ward to attend an out-patient department should be discontinued; if it is essential for the patient to attend the out-patient

department, the surgeon in charge of fractures should also be an out-patient officer.

The treatment of fractures should be discussed in the light of the British Medical Association report by the surgical staffs of all large teaching hospitals. In the country it ought to be considered by subdivisions of the Branches of the British Medical Association, where they exist, and by local medical associations where there are no subdivisions. A great deal has been written in the British Medical Association report on the economic side of the subject. In the present state of industrial organization the fracture problem is almost entirely a surgical one; it therefore behoves the medical profession to organize its ranks and give to the community the service to which it is entitled.

Current Comment.

EXERCISE IN HEART DISEASE.

THERE is discernible in the therapeutics of recent years a certain tendency to return to simple methods, and although the resources of science are used so far as is possible, it is realized that complexities are best eliminated, especially in the case of chronic disease. One example of this is in the treatment of chronic heart disease, where we know that after an accurate diagnosis is made it is still necessary to translate into the simplest terms the ideal life for the patient. Moreover, he must learn just how much it is necessary for him to rest and to what degree to take exercise, and, this is a vital point, the doctor should be able to tell him how much exercise is safe or desirable. The patient himself sometimes asks: "How can I strengthen my heart?" This question is not easy to answer, and cardiologists have recently been turning their attention to this apparently simple problem. Is it possible to add to the cardiac reserve by a system of training in the case of those suffering from an actual disease of the heart? There is, indeed, a good deal of argument still on this topic, and competent authorities have been known to hold divergent views, as S. H. Proger and C. Korth point out in a contribution on the subject of the effect of light muscular training on patients with heart disease.¹

Some of the experimental work extant on the subject is not very convincing. Purely subjective evidence is not satisfactory, as every clinician knows, for the degree of inadequacy of the heart is not always paralleled by the presence or absence

of subjective dyspnoea, for example, in the patient. Proger and Korth studied six patients and two controls for a training period of six weeks, during which the subjects of the experiments performed exercises on a stationary bicycle fitted with a heavy flywheel and an adjustable brake. In some cases shorter or longer periods were used, according to the circumstances of the patients; for instance, one patient suffered an haemoptysis during the exercise, which was naturally abandoned. The patients were all young, between the ages of eighteen and twenty-two years. They had rheumatic heart disease; three had mitral lesions, and the other three combined mitral and aortic lesions. One only had a disturbed rhythm, with auricular fibrillation. Before and after the training period frequent observations were made of the pulse and respiration rates, oxygen consumption, respiratory minute volume, cardiac output, velocity of blood flow, vital capacity, and breath-holding capacity; and electrocardiographic and radiological observations were made. During exercise changes were observed in the pulse and respiration rate, respiratory volume, blood pressure, oxygen consumption, blood velocity, and lactic acid in the venous blood. The objective findings in this series of experiments would be regarded as adequate for the formation of an opinion on the effect of exercise. The results showed that there was a slight improvement in the normal subjects and a very definite improvement in the patients who had a double valvular lesion. The patients with mitral stenosis showed no improvement of any notable degree; one, indeed, became worse, showing a slight decline, culminating in haemoptysis. In the case of two of the patients who showed an improvement the vital capacity increased to a perceptible extent. This was not observed in the normal controls, however, who showed no change. Another constant change for the better in the improved patients was a slowing of the blood velocity at rest, and it was also observed that the pulse rate and the oxygen consumption ran parallel in every case to a striking degree. One experimental finding that is worth recording is that there was not uncommonly a certain degree of spontaneous fluctuation of the pulse rate either at rest or after exercise. The bearing of this on the common exercise tolerance tests as carried out in the ward or consulting room will be apparent and, as is the case with most tests used in clinical medicine, too much reliance should not be placed upon the results of a single reading.

The lack of consistency in the results of this experiment is not easy to explain in this series, small though it is. It certainly would appear that the pure mitral lesion is not amenable to improvement by training, possibly because it is more difficult to obtain an adjustment between the greater and lesser circulations in these cases. Clinically, as the authors point out, the coexistence of an aortic lesion seems to be to the advantage of the patient with mitral stenosis, provided the defect be not too large. Proger and Korth conclude that

as the result of this experience they are not prepared to predict what type of patient will improve with light exercise. They discuss the factors that may be involved, such as improvement in vital capacity and cardiac efficiency and enhanced neuro-muscular efficiency through practice. The latter is well known, for there are many instances in which patients with well developed heart disease are able to carry out certain types of exertion well, through long practice, but are liable to fail when work of another kind is attempted. The whole subject of physical training is by no means worked out. There are many interesting features that have never been quite fully investigated. For example, it is well known that when an athlete attempts what is known as a "come-back" after a long absence from the arena, a long period of training is necessary. This lesson may well be taken to heart when it is attempted to improve the condition of "cardiac" subjects after a prolonged period of forced inaction, and in the light of present knowledge it may be said that it is worth while to make an effort to improve the physical efficiency of such patients, but it must be made with great caution and adequate safeguards.

ARTIFICIAL PNEUMOTHORAX IN THE TREATMENT OF LOBAR PNEUMONIA.

DURING recent years considerable discussion has taken place regarding the induction of artificial pneumothorax in the treatment of lobar pneumonia. Some authors, reporting small series of cases in which the method was used, have advocated it. Others have opposed its use. It is therefore of interest that F. G. Holmes and H. Randolph have reported the induction of artificial pneumothorax in eighteen cases of pneumonia.¹ The oldest patient was thirty-six years of age and the youngest three; eight were over and ten were under twelve. Five of the eight adults had adhesions, but in none was adequate collapse prevented. Five of the ten children had adhesions; in two the adhesions were so dense that only a small amount of air was injected; both these patients subsequently died of empyema. In two children, not included in the series, adhesions prevented the introduction of any air at all. These authors find that the induction of artificial pneumothorax reduces the pain caused by pleurisy and increases the depth of respiration. They hold that it lessens toxæmia, a hazardous deduction, probably, from so small a series. They state that it seems probable that the duration of pneumonia is shortened and that at times the crisis is brought about with dramatic suddenness. They think that the danger of spontaneous collapse and empyema is increased in children. In their opinion total mortality is decreased by the use of pneumothorax, the incidence of late complications is probably reduced, and spreading involvement of new lobes is checked. Whether these conclusions are justified or not, there is justification for further trial of the treatment.

¹ *Annals of Internal Medicine*, March, 1935.

Abstracts from Current Medical Literature.

PHYSIOLOGY.

Voluntarily Induced Increases in the Rates of Certain "Involuntary" Physiological Processes of a Human Subject.

IN a series of measurements of basal metabolism over long periods of time and with a variety of subjects, unexplainable variations in the range of metabolism, either on the same day or on different days, are occasionally found. T. M. Carpenter, R. G. Hoskins and F. A. Hitchcock (*American Journal of Physiology*, December, 1934) record a complete study of one of themselves (R.G.H.), who believed that he could alter voluntarily the rate of oxygen consumption without an observer being aware that any effort was being made to change the physiological processes. This belief was based in part on the knowledge that his pulse rate and systolic blood pressure were in considerable measure amenable to voluntary control. The total respiratory exchange, pulse and respiration rates, and systolic and diastolic blood pressures were determined in the typical "basal" post-absorptive condition and in five- and ten-minute periods, during which he voluntarily produced an increase in all the factors without visible effort. The increases produced were from 13% to 32% in the oxygen absorption, 17% to 26% in the pulse rate, 9% to 28% in the systolic pressure, and 4% to 27% in the diastolic pressure. The basal metabolism varied from -9.0% to -10.9% (Harris-Benedict standards) in the normal periods, and nil to 24.9% in the periods of voluntary increase. These changes were independent of emotion and independent of changes in skeletal muscle tonus. This latter, a conscious perception of the subject, was verified by palpation. The authors admit that it is difficult to explain how the augmentation of the various "involuntary" processes is induced, but consider that it is probably no more and no less mysterious than is, for example, the flexing of a biceps muscle. One simply "wills" the change and it takes place. A striking phenomenon associated with the experiments was a subjective sense of rather marked fatigue at their conclusion. This may possibly have been due to the difficulty of "forcing" nerve impulses into unaccustomed channels. A similar state of affairs is seen when, by the injection of adrenaline, a picture of sham emotion is set up. The observation periods were carried out in succession according to a schedule previously arranged with the subject. During the last period of one series the subject made an effort to produce as large a change as possible. It was his purpose not to inhibit muscle tonus, but to

maintain an unchanged posture so that the tonus would not be readily perceptible to the observers. The changes produced during this period were not so very much greater than the changes produced when the muscles were flaccid. That the augmented oxygen absorption was not in any significant degree dependent upon increased respiratory effort is suggested by the fact that in the fourth experiment the respiratory rate was even decreased. The relative rise in the respiratory quotient in all of the experiments was not so great for the most part as in the other factors. Although it may be considered that the changes were in part ascribable to static work, it must be noted that if the observations had been made in the usual way, with the subject covered by a blanket, it would have been impossible to have detected any changes, and the observations would have been considered as having been made under true basal conditions. The authors emphasize the extreme care which must be used in supervising and controlling these tests.

Normal Metabolism in Old Age.

THE relationship between age and basal metabolism is known with considerable certainty for normal patients of twenty to sixty years of age, but the available data for childhood, puberty and old age, particularly beyond the age of seventy, are not very convincing. James R. Matson and F. A. Hitchcock (*American Journal of Physiology*, December, 1934) have carried out a series of basal metabolism tests on eight women ranging in age from 77 to 106 years, and on 14 men whose ages ranged from 74 to 92. The determinations were made with the closed circuit type of apparatus known as the Benedict Roth. The oldest subject, a woman of 106 years of age (incidentally the oldest human being whose basal metabolism is recorded), 147 centimetres tall and weighing 31.8 kilograms, had a total heat production of 23.81 calories per hour. She produced 0.749 calorie per hour per kilogram of body weight, and 21.07 calories per square metre of body surface per hour. Six of the female subjects, with an average of 82.5 years, gave the following averages: total heat production, 43.65 calories per hour; calories per hour per kilogram of body weight, 0.74; calories per hour per square metre of body surface, 27.43. The fourteen men, whose average age was 81.6 years, gave the following averages: total calories per hour, 50.38; calories per hour per kilogram of body weight, 0.82; and calories per hour per square metre of body surface, 30.11. The experimental results were compared with the Harris-Benedict, Aub-Du Bois and Dreyer standards. The results on the female subjects were well below all of these standards, although the best agreement was obtained in the case of the Harris-Benedict standards. With the

men the agreement with the Harris-Benedict standards was fairly satisfactory, but the other two standards gave figures much higher than the experimental results. The difference between the sexes was of approximately the same magnitude as that for adults of less advanced age.

Denervation of the Carotid Sinuses and Section of the Depressor Nerves as a Method of Producing Arterial Hypertension.

ACCORDING to some observers it is possible to obtain a durable arterial hypertension uncomplicated by destructive lesions of important viscera. By denervating the carotid sinuses and sectioning the depressor nerve in rabbits, Koch and Mies (1929) and Kremer *et alii* (1933) obtained an arterial hypertension which they state persisted as high as 170 millimetres of mercury for two years. Heyman and Bouckaert reported similar results in dogs following the same type of operation. M. F. Green, Albert F. Degroat and C. H. McDonald (*American Journal of Physiology*, January, 1935) were able to demonstrate an immediate hypertension, but it appeared to be relatively transient. They report the effects of denervation of the carotid sinuses and section of the depressor nerves in a series of twelve rabbits, and of denervation of the carotid sinuses and section of the cardiac fibres of the vagus nerve in a series of nine dogs. In the rabbit the sinuses were denervated and the depressor nerves cut, either at the same operation or in two stages. Denervation was accomplished in both rabbits and dogs by stripping away all connective tissue from the carotid bifurcation and along each vessel, painting the surfaces with an 85% solution of phenol and then washing with alcohol. These authors claim that the operation adopted in dogs permits complete and certain section of the four vaso-sensory nerves, allows definite survival of the animal, and is almost without mortality. It is performed in three stages: (i) anterior transpleural section of the right cardiac nerves, (ii) denervation of the carotid sinuses as described, (iii) section of the left vagus nerve in the neck. Twelve dogs were operated on in this manner with entirely uniform results. Following the above cited operation in rabbits a transient elevation of blood pressure was observed. There was no increase in respiratory rate and no sudden deaths occurred. In dogs the operation described was followed by an unstable blood pressure, which tended after a variable period of time to become stabilized at a level not greatly above normal. Three dogs died of what appeared to be acute cardiac failure at varying periods of time after operation. In some dogs a tachycardia which is similar or identical to the tachycardia of vagotomy alone followed this operation. The pulse rate in rabbits was not

followed. After this operation in dogs there was no increase in respiratory rate.

The Effect of Oxygen on Man at Pressures from One to Four Atmospheres.

A. R. BEHNKE, F. S. JOHNSON, JOHN R. POPPEN AND E. PREBLE MOTLEY (*American Journal of Physiology*, January, 1935) present experimental data showing the tolerance of man to oxygen at pressures of one, two, three and four atmospheres. Healthy men between the ages of twenty-two and forty were used as subjects. Three groups of experiments were performed. In Groups I and III the subjects sat in a chair and breathed commercial oxygen through a mask connected with a Benedict apparatus. For pressures in excess of one atmosphere the large pressure chamber described by Thompson Yagion and Van Wart was used. In Group II the subject reclined on a cot and, with his head placed in a helmet, breathed commercial oxygen at atmospheric pressure. The subjects studied could breathe pure oxygen with comparative safety as follows: four hours at one atmosphere, three hours at two atmospheres, two hours at three atmospheres. The symptoms induced were referable mainly to the nervous system. At four atmospheres' pressure convulsions occurred in one subject and syncope in another after exposures of approximately forty-five minutes. Only two subjects were tested at this pressure, at which the oxygen in physical solution (approximately seven volumes per centum) is sufficient to satisfy the tissue requirements, and at which, therefore, the most striking effects of oxygen are seen. At a pressure of one atmosphere, impaired nervo-muscular coordination and power of attention, or an increased effort to maintain these functions, occurred after one to three hours' exposure in three out of four subjects tested. Hyperpnoea occurred after three hours' exposure to oxygen in two out of eleven subjects. The irritative effect of oxygen on the lungs was noted in only one subject on a single occasion. The symptoms were substernal pain, dry cough and a high leucocyte count. The subjects exposed to the higher oxygen pressures were singularly free from pulmonary symptoms. Oxygen consumption is high during the first twenty minutes and then decreases to a level which is constant for periods up to four hours at atmospheric pressure. In all of the oxygen exposures the blood pressure, the respiratory rate and the minute volume (with two exceptions) were constant at one, two, three and four atmospheres' pressure.

BIOLOGICAL CHEMISTRY.

Œstrogenic Substances in Urine from Pregnant Women.

S. L. COHEN AND G. F. MARRIAN (*Biochemical Journal*, Volume XXVIII, Number 4, 1934) have utilized the

Kober reaction for the quantitative estimation of œstrone (ketohydroxyœstrin or theelin) and œstriol (trihydroxyœstrin or theelol) in human urine from pregnant women. The greater part of the œstrogenic material in the urine of pregnancy is œstriol. It is claimed that the quantitative colour test used is as accurate, if not more accurate, than the biological assay, and can be carried out in a very short time, whereas the biological method requires several days. After hydrolysis with hydrochloric acid at pH 1 to 2 in an autoclave at fifteen pounds pressure for two to four hours, the urine is cooled and extracted with ether. The ethereal extracts are washed with aqueous sodium carbonate, and from the ethereal extracts the œstriol is removed by extraction with N/10 sodium hydroxide. The ether residues now contain the œstrone and are evaporated to dryness, and the residue is taken up in toluene, from which the œstrone is removed by extraction with normal sodium hydroxide. The two separate sodium hydroxide extracts are saturated with carbon dioxide and then extracted with ether. The ether extracts are evaporated to dryness, the residues are dissolved in alcohol and aliquots of this solution are used in the colorimetric assay. The sample for assay is evaporated to dryness at 100° F. under a stream of nitrogen. To the residue are added two cubic centimetres of phenol-sulphonic acid reagent. The mixture is heated for ten minutes at 100° F., cooled in a freezing mixture, made up to four cubic centimetres with 5% sulphuric acid, and the colour analysed in a Lovibond tintometer.

Colloidal Gold Reaction for Neurosyphilis.

W. C. MENNINGER AND L. BROMBERG (*Journal of Laboratory and Clinical Medicine*, January, 1935) have described the results of the application of the colloidal gold reaction to 500 unselected cases of neurosyphilis. In each case the clinical diagnosis was supported by a positive Wassermann test on the cerebro-spinal fluid. The authors found no correspondence between the pattern and degree of precipitation and the type of central nervous system involvement. They consider that the colloidal gold curve is in itself not diagnostic, though of considerable confirmatory value in the presence of clinical signs of general paresis.

Detection of Pathological Amounts of Lead in the Peripheral Blood.

H. BLUMBERG AND T. F. MCNAIR SCOTT (*Bulletin of the Johns Hopkins Hospital*, January, 1935) have developed a spectrographic micro-method for the detection of pathological amounts of lead in the peripheral blood. Only 0.1 cubic centimetre of blood is needed. The lead line at 2833-07 A.U. does not appear visible to the naked eye until the concentration of lead rises above

0.1 milligramme per 100 cubic centimetres (that is, until it reaches the pathological range of approximately 0.2 to 1.0 milligramme per 100 cubic centimetres). The method has been found useful for the rapid diagnosis of lead poisoning. The entire analysis can be completed in thirty minutes. It is claimed that a negative result eliminates lead poisoning as a diagnostic consideration.

Lipoid Chlorine in Serum.

J. P. PETERS AND EVELYN B. MAN (*Journal of Biological Chemistry*, October, 1934) have demonstrated that small amounts of chlorine can be extracted with the lipoids by petroleum ether from normal serum. The fact that chlorine could not be extracted with the lipoids from bacon or butter appeared to indicate that chlorides are not rendered soluble in petroleum ether by the presence of lipoids. Lipoid chlorine was found to be increased in the sera of patients with the nephritic syndrome who have hyperchloræmia and hyperlipæmia. That the lipoid chlorine is not diffusible (and therefore possibly incapable of forming salts with base) was indicated by the observation that no chlorine could be extracted by this procedure from artificial ultrafiltrates, and only minute quantities from serous transudates. The authors suggest "that the occurrence of unusually large amounts of lipoid chlorine in the serum may afford an explanation for the hyperchloræmia that is so often observed in patients with the nephritic syndrome, at times when they exhibit no signs of impairment of the ability to excrete inorganic chloride". Further, the presence of the lipoid chlorine may explain the observed fact that the base-combining equivalents of protein, bicarbonate, chloride and inorganic phosphate sometimes definitely exceed the sum of the bases sodium, potassium, calcium and magnesium. Such discrepancies were usually encountered in patients with nephritic syndrome.

Essential Amino-Acids.

In experiments with rats, Madelyn Womack and William C. Rose (*Journal of Biological Chemistry*, November, 1934) have shown that absence of phenylalanine and tyrosine from a diet otherwise complete, results in nutritive failure. When phenylalanine was added to the diet, growth was just as good as when both amino-acids were supplied. When phenylalanine was replaced by tyrosine, a rapid loss in body weight invariably followed. The authors conclude that, contrary to the usual belief, phenylalanine is an indispensable dietary component, and that tyrosine is quite unable to replace it under the experimental conditions employed.

R. S. ALCOCK (*Biochemical Journal*, Volume XXVIII, Number 4, 1934) has shown that tyrosine is not an essential dietary component. The tyrosine was removed from protein hydrolysates by the enzyme tyrosinase.

Public Health.

PUBLIC HEALTH WORK AND METHODS IN VARIOUS COUNTRIES.

THE following is the text of a report by Dr. A. R. Southwood, head of the Department of Public Health, South Australia, of an inquiry into public health work and methods in various countries. The report bears the date January 24, 1935. Part of this report appeared in the issue of April 27, 1935.

VENEREAL DISEASES.

English Methods of Control

The Venereal Diseases Scheme in England has been in operation since 1916. The present policy and practice of the Ministry of Health in respect of venereal diseases are based largely on the recommendations of the Royal Commission on Venereal Diseases in 1916. Among other things, the commission recommended: (a) the extension of facilities for diagnosis; (b) the provision by local authorities of means of free treatment for all classes at convenient hours and under suitable conditions; (c) improved education of the general public and of medical students in venereal diseases; (d) the prohibition of all advertisements of remedies and of unqualified practice.

The commission opposed the compulsory notification of venereal diseases and condemned "unqualified practice" by chemists, herbalists and others as "disastrous" and "one of the principal hindrances to the eradication of those diseases". It was considered that compulsory notification would cause many patients to avoid reporting for treatment. It was further stated that "the most urgent requirement is to secure to every patient the freest and earliest possible access to medical assistance when there is suspicion of venereal disease. This implies, *inter alia*, that all temptation for the patient to have resort to an unqualified person shall be removed."

The scheme of the British Ministry of Health is therefore based on the principle that treatment is primarily to prevent the spread of the diseases, that it is for the benefit of the community as well as the individual, and that ample facilities for free treatment should be available to every sufferer. The county and county borough councils have set up a large number of treatment centres and have also carried out, either directly or through the agency of the British Social Hygiene Council, a more or less continuous education of the public.

According to Sir George Newman (1933), the indications are that, in respect of syphilis, the scheme has been attended by a considerable measure of success. He says that the majority of persons infected with syphilis in England report to the treatment centres early and that the people generally realize the seriousness of the disease and the danger of infecting others. Early and efficient treatment has rendered the occurrence of the severe external mutilations of the later stages of syphilis a rarity. It seems, too, that the incidence of syphilis has fallen during the last few years. In 1930, 18,833 sufferers reported for the first time at treatment centres; in 1933 the number was 16,767. Gonorrhoea, however, presents another story. The returns show no decline in its incidence. Nor is the situation likely to improve until a specific remedy is found and until infected persons fully realize the importance of thorough treatment.

Notification of Venereal Diseases.

In England venereal diseases are not notifiable. I discussed the matter with officials of health departments and of the British Social Hygiene Council, and with several private practitioners. The general view is that compulsory notification would not achieve more than is being done under present conditions and, what is worse, would probably cause many sufferers to refrain from or delay in reporting for treatment. It is considered a better plan to

encourage early and adequate treatment of sufferers by providing good and ample facilities and by having these free clinics available at all hours.

Education in sex hygiene is considered desirable, and much valuable work in this direction is being done, especially by the British Social Hygiene Council. The dissemination of information regarding prophylactic treatment and the provision of materials for its performance are not favoured by most English authorities. Emphasis is rather placed on the necessity for sufferers to apply for treatment at the first signs of disease.

In the United States of America venereal diseases are notifiable. The Venereal Diseases Section of the Federal Health Department publishes a monthly journal in which current medical work on the subject is reviewed, and it distributes the journal to medical practitioners and to local authorities. Until recently subsidies were paid by the Federal Department to assist local authorities in providing treatment centres.

In Canada the measures for dealing with venereal diseases differ from the British system. Commenting on this, Sir George Newman, Chief Medical Officer, British Ministry of Health, says:

The British system relies wholly on persuasion and attraction to secure treatment of the infected; it depends entirely on the effectiveness of its propaganda and on the quality of the treatment provided at its clinics. In most provinces of Canada and states of America, on the other hand, propaganda and facilities for treatment are supplemented by notification and compulsory treatment of those suspected of conveying infection, and in America there are laws for the repression of prostitution. In both Canada and the United States considerably more of the treatment is carried out by private practitioners, but these notify only a small proportion of the cases under their care.

Provision of Free Treatment.

Free treatment for sufferers from venereal diseases is available in most countries. In England, for instance, everyone, rich or poor, may claim gratuitous treatment for venereal disease at the clinics. Most countries also provide free laboratory facilities, and serological and bacteriological investigations are carried out for private practitioners free of charge. In England only registered medical practitioners are permitted to treat sufferers; unqualified practice by pharmacists and others is illegal.

In some countries arsenical preparations are issued free to private practitioners for the treatment of venereal disease, but this is hardly necessary if free treatment is provided at clinics.

British Social Hygiene Council.

I attended, by invitation, the annual conference of the British Social Hygiene Council held in London in July. A number of English and overseas members were present. The Right Honourable L. S. Amery, M.P., opened the conference and described the work of the Council. The most striking address was that of Colonel L. W. Harrison, of the British Ministry of Health, who gave a masterly review of the venereal diseases situation and outlined modern methods of treatment. Other speakers discussed the value of instruction in biology in schools and considered that such instruction provided a basis for proper living. The treatment of seamen suffering from venereal disease and the problem of prostitution were also discussed.

The whole function of the council is to educate the public in matters of sex hygiene. The ideal of the Council is a clean nation and a clean empire. In the work it sets out to do the council appears to be fulfilling a highly useful function. It is supported by voluntary contributions and by subsidies from local authorities. Vigorous instruction of the general public is given as to the nature and dangers of venereal infections and the necessity for proper treatment by qualified practitioners is repeatedly stressed. I am convinced that carefully planned and properly conducted efforts in teaching the people along these lines produce better results than compulsory

notification. To lead the people in the way of health by teaching them seems to me a sounder plan than to try to drive them by compulsory measures.

The venereal diseases problem is far more than a purely medical one. It presents much greater difficulties than the control of, say, diphtheria or smallpox. Indeed, when the attempt is made to eradicate venereal diseases it is found that many of the problems are not medical at all, but are economic, social, psychological, religious, sentimental and legal. These are all intricate problems of the greatest difficulty.

FOOD AND DRUGS CONTROL.

Nutrition and National Health.

The responsibility for insuring that the people shall be supplied with wholesome foodstuffs has become accepted the world over as a government one. Professor J. B. Orr, Director of the Rowett Research Institute, put the matter succinctly in his Chadwick Lecture that I attended in London in June. He said that:

A regular daily supply of food is necessary for the continued life of the community The maintenance of the food supply is one of the most important duties of a Government Indeed, the State has assumed the responsibility for seeing not only that the supply will be sufficient for the Nation as a whole, but that each member of the community shall have sufficient.

In England the Ministry of Health has long insisted upon the vital importance of nutrition as a fundamental factor in personal and public health. Investigations have been made into the effects of malnutrition, and especially into the various effects of vitamin and other food deficiencies. The Medical Research Council has sponsored special researches into such matters as the nature and constitution of vitamins, dental disease and the influence of diet on resistance to bacterial infection. At the Rowett Research Institute at Aberdeen, I saw work in progress on animal nutrition, vitamin dietary deficiency and the function of various mineral salts in nutrition.

In schools in England it has become the custom to an increasing extent to issue small bottles of milk, one-third of a pint, to each child. In the London County Council schools, for instance, it was found in October last that 364,000 children were being supplied with milk daily. In most cases the issue is made free to the children, the cost being borne by the council. Free meals are also made available to poor children in these schools.

"Nutrition and Disease" was the subject of several papers presented before the British Association Meeting at Aberdeen in September, 1934. In concluding the discussion, Sir Frederick Gowland Hopkins, President of the Royal Society, stressed "the national importance of this diet question". Professor Orr spoke of good nutrition as a factor in promoting good resistance to disease, and of the need for the proper dieting of expectant and nursing mothers, and of infants. Professor S. J. Cowell, of Saint Thomas's Hospital, London, referred to "giving milk to school children not (as) an experiment, but just the right thing to do".

Safeguarding Foodstuffs.

Two principal methods are adopted to assist the people: (a) the education of the community in the principles of dietetics and in the choice of suitable food; and (b) the safeguarding of food from deficiencies in composition, from adulteration, and from contamination. In the Ministry of Health laboratories chemical and bacteriological examinations of foodstuffs are continuously being conducted. Further, the administration of meat, milk, and important food regulations, tuberculin testing of milk herds, and the supervision of food premises are among the routine methods by which the purity of food is maintained. Similar activities are also pursued by local authorities throughout England.

In the United States of America the Food and Drug Department of the Federal Government is under the control of the Department of Agriculture, and collaborates with the Public Health Service. At the central laboratories in Washington and at other cities a large staff of scientific

workers is continuously employed studying the various problems relating to food. Federal officials have jurisdiction over only such commodities as enter interstate or foreign commerce. They have no jurisdiction over articles produced and sold within the confines of a single State. Most of the States, however, have laws similar to the federal acts, and in some States federal legislation on food and drugs is automatically adopted into the State legislation.

In Canada the Dominion Government Department of National Health controls extensive and well equipped laboratories at Ottawa for the continuous investigation of foods and drugs. Sera and other biological products are carefully analysed by physiological and biochemical methods. Such work requires much apparatus and a highly trained staff of experts. It can be done only in a large way.

Meat Inspection, Slaughtering and Transport.

For several years the Ministry of Health in England has been endeavouring to improve the general standard of meat inspection throughout the country. The efficient supervision and control of meat supplies is considered by English authorities to be impossible unless there are central public abattoirs where adequate inspectorial services are provided. It is observed regretfully by Sir George Newman that in England there are only 112 such public abattoirs, while some 16,000 private slaughterhouses exist. Many progressive local authorities are providing public abattoirs, and it is hoped others will follow the example. At Croydon no private slaughterhouses are permitted; all slaughtering is done in the Council Abattoirs, and all the meat is carefully inspected.

This matter of meat inspection is of great importance to us in Australia, for imported food is carefully inspected in England. Careful watch is kept at all ports on foodstuffs imported from abroad, and, although the quality of the food landed is generally high, it sometimes happens that foodstuffs, especially meat, are condemned on arrival in England. The last few years, I am informed, have shown a marked improvement in the quality of food entering England from overseas.

Dr. Willoughby, Medical Officer of Health, City of London, who directs meat inspection at the huge Smithfield Market, informed me that caseous lymphadenitis was occasionally found in meat imported from Australia and New Zealand. He said that during the last two years the inspection of carcasses at the place of slaughter appeared to have been more efficient, and less evidence of disease was found on arrival of such meat in London. There has been little improvement in the inspection of "quarters" and "pieces".

Great advances have been made in recent years in the long distance sea transport of meat, especially in the process of "chilling" as distinct from "freezing". Frozen meat is carried at 15° F. It keeps well, but becomes materially altered and toughened by the freezing. Chilled meat is carried at a constant temperature of 29° F., and the atmosphere of the cooling chamber is kept charged with carbon dioxide gas at a constant concentration of 10%. The purpose of the added gas is to prevent mould development and bacterial growth. The motor vessel, *Port Fairy*, on which I travelled to England, carried a cargo of chilled beef under these conditions. This was in the nature of a "field work" experiment, scientifically directed by the Low Temperature Research Station in Cambridge. During the voyage the temperature of each chamber was carefully recorded every four hours, indeed the carcasses were treated as tenderly as a set of patients in hospital, and the records were handed to the research workers on arrival in England. So far it has been found possible to carry chilled meat quite satisfactorily for sixty days, and at the end of that period the meat is perfectly sound and practically indistinguishable from fresh meat.

Food Poisoning.

Cases of food poisoning are notifiable in London, and are carefully investigated, a large amount of the work being done in the Ministry of Health's pathological laboratories. Work of a highly scientific and valuable nature has been

done, especially in the isolation and identification of the *Salmonella* type of organisms.

The idea that people developed food-poisoning from eating "ptomaines" or toxins that formed in decomposed meat and other foods has been abandoned for some years. Investigations have shown that in practically all cases of food-poisoning some bacterial contamination is the underlying cause. Most recent research work on the subject has related to the various types of bacteria and other organisms likely to occur as contaminants.

Metallic poisoning, as from arsenic or lead, is also responsible for severe illness in some instances. Cases of antimony poisoning have recently occurred from drinking lemon juice that had been mixed and allowed to stand in enamelled vessels. Antimony is sometimes used as an opacifying agent in surfacing enamelled ware, and the metal is dissolved by acid fluids.

Control of Narcotic Drugs.

In most countries legislation now exists designed to control the misuse of narcotics and other dangerous and habit-forming drugs. The subject has received much attention from the Health Organization of the League of Nations, and the aim has been to unify the various *Dangerous Drugs Acts* so that satisfactory international control may be obtained.

In England the *Dangerous Drugs Acts* are administered by the Home Office. In the United States the control is exercised by a separate division of the Treasury Department, and in Canada the Department of Health is responsible for the work. In each of these countries great activity is displayed by the authorities concerned.

Heroin (diacetylmorphine) is considered the worst of the habit-forming narcotic drugs, and the League Organization is making vigorous attempts to combat its dangers. In the United States the manufacture and therapeutic use of heroin is now prohibited. Although the drug is very valuable in medical treatment, it is found that other less harmful substances are now being evolved to take its place.

MILK.

Importance and Attainment of a Pure Milk Supply.

Nutrition authorities are agreed that a greater consumption of milk is the most desirable of all dietetic developments from the point of view of the better health of the community. A high value is set on the nutritive properties of milk, especially in the dietary of children. In many centres in England, and in New Zealand, the free daily issue of milk to school children is now an established practice. Efforts are being made in many countries to get the people generally to "drink more milk". It is difficult, however, to increase the consumption of milk to any appreciable extent unless people can be convinced of the purity of the supply. Everyone knows that milk may become contaminated by disease-producing germs, and that illness may arise from drinking the infected milk. To obtain pure milk for the people, the obvious prime need is healthy herds of dairy cows, and even then it is only by the exercise of scrupulous cleanliness on the part of milkers and distributors that the purity of supply can be maintained.

The milk trade is a complex one. The size of retail businesses varies from that of large combines, such as United Dairies in England, to that of small businesses with a daily turnover of a few gallons. Milk may be sold loose or in bottles; it may or may not undergo a number of processes, such as filtering, cooling, and heat treatment; it may be transported great distances before sale, or it may be consumed where produced.

In big cities, such as London, the large concerns hold the bulk of the trade. Although there are about 3,000 milk vendors' licences issued in the London area, it is estimated that 80% of the milk is sold by three large companies, and about 12% by ten smaller ones. The milk is produced mainly in distant country centres, where local collecting stations are established for the cooling, filtering and bulking of the milk. The bulked milk is transported

either by rail or road in glass-lined tanks of 3,000 gallons capacity to the consuming centre. United Dairies have in London five large depots, where the milk is pasteurized, and either bottled and sold directly at retail, or resold in bulk at wholesale.

In New York city, 99% of the milk sold is pasteurized. The daily consumption is three million quarts. The small quantity of milk not pasteurized is produced under strict medical supervision; it is sold as "certified milk", and commands two or three times the price of pasteurized milk. The city employs its own officers to inspect the supplying dairies, some of which are 200 miles away.

The City of Wellington is unusual in its municipal scheme for the handling of milk. An agitation by farmers that the city authorities should take control of the vending of milk led to the passing of a special act in 1919. The City of Wellington now owns a large refrigerating and pasteurizing plant; it buys milk from the surrounding farmers, treats it, and retails it in the city. A careful system of testing the milk and of farm inspection is carried out constantly, about £1,500 per annum being spent on this aspect of the work. Although the city authorities control this scheme, nearby farmers, within two miles of the city, are still allowed to retail milk within the city boundaries. At the present time about 5,000 gallons of milk, all pasteurized and bottled, are sold by the City Milk Department each day, while nearby farmers still retail about 3,000 gallons of raw milk daily in the city.

Cattle Diseases and the Public Health.

In England, the concern of the Government for the welfare of the dairy industry and for the people's health led the Economic Advisory Council to appoint an influential committee, with Sir Frederick Gowland Hopkins as chairman, to investigate cattle diseases. The report published in May, 1934, clearly describes the conditions in England, and makes suggestions for improvement.

The main diseases reviewed by the Committee's report are bovine tuberculosis, contagious abortion, Johne's disease, and mastitis. It is stated that at least 40% of cows in dairy herds are infected with tuberculosis, but fortunately only a small proportion of tuberculous cows give infected milk. The general view appears to be that cattle are infected with contagious abortion to about the same extent as with tuberculosis. The incidence of Johne's disease is uncertain; it is probably not great. Mastitis, the infection of the udder by several kinds of bacteria, affects about 30% of the milking cattle of England.

Milk may be dangerous to public health, either because it is infected when yielded by the cow, or because it is contaminated during milking or subsequently. Tuberculosis, contagious abortion, and certain forms of mastitis are dangerous to man, the associated human diseases being respectively tuberculosis (principally non-pulmonary), undulant fever, and occasionally in the case of mastitis certain epidemic diseases, such as streptococcal sore throats.

The Committee's report emphasizes that the inspection of dairy cows, the supervision of milking premises, and of all places where milk is treated and bottled, and, indeed, the whole series of steps from cow to consumer, must be constantly under control. It is also considered that all milch cows should be inspected by competent veterinary surgeons at least three times a year.

The Committee gave special attention to tuberculosis. Bovine tuberculosis in human beings is attributable to infection from milk, the food of childhood. The disease causes over 2,500 deaths each year in Great Britain. The total eradication of bovine tuberculosis from all herds is the only complete solution of the problem of tuberculous milk. Thorough clinical inspection of cows reduces the amount of tuberculous milk passing into consumption, but it can never render the milk supply safe.

In London, an investigation by the London County Council showed that 3.2% of samples of milk retailed are infected with tubercle bacilli. At Croydon, 288 samples of unpasteurized milk showed tubercle bacilli in ten, while 132 pasteurized samples gave no tubercle bacilli.

The Tuberculosis Order of 1925, which extends to the whole of Great Britain, requires that animals yielding tuberculous milk, or showing clinical signs of tuberculosis, should be notified to the local authorities, and by them slaughtered, subject to the payment of compensation. In recent years the number of animals slaughtered annually under this order was between 15,000 and 19,000, and the compensation paid has amounted to between £60,000 and £70,000 a year. The Ministry of Agriculture pays three-quarters of the compensation, the local authority concerned one-quarter.

The fact that the Ministry of Health in England received reports on the tuberculin testing of more than 18,000 cattle during 1933 gives an indication of the extent to which this practice has been adopted in England.

In Massachusetts (United States of America) tuberculin testing of cattle is extensively carried out. Beasts giving a positive result are destroyed, and the owner is compensated to two-thirds the assessed value, the expense being shared equally by the State and Federal Governments.

The Grading of Milk.

By the Milk (Special Designations) Order, the Government in England provided for the grading of milk. The Order recognizes the following four grades: (a) Certified milk, or raw milk from herds free from tuberculosis. It must be bottled on the farm. (b) Grade "A" tuberculin-tested milk is raw milk from non-tuberculous cows. It may be bottled on the farm or elsewhere. (c) Grade "A" milk is from cows which have passed a quarterly veterinary examination. It may be raw or pasteurized. (d) Pasteurized milk is milk which has been retained at a temperature of 145° to 150° F. for at least thirty minutes.

Besides these special grades, there is just plain "milk". There is not a great demand for the designated milk in England. The sales are far below the supply.

The Committee on Cattle Diseases has proposed new regulations governing the grading of milk and pasteurization. It proposes that:

All milk sold for consumption in liquid form should be required to be sold under an official designation . . . No milk should be sold that does not attain a fixed standard of cleanliness at the farm. This standard should approximate to that at present required for Grade "A" milk. In addition, all milk should conform to the definitions of one of the following designations:

(i) Certified milk, namely, milk which has not undergone any process of heat-treatment, and is derived from tubercle-free herds.

(ii) Pasteurized milk, namely, milk which has undergone, once only, a process of heat-treatment approved for this purpose by the Ministry of Health or the Department of Health for Scotland, and has undergone no other process of heat-treatment. Pasteurization should be permitted only in a plant licensed for the process.

(iii) Sterilized milk, namely, milk which has been raised to the boiling point or higher in a plant licensed for the purpose, and which has undergone no other process of heat-treatment.

(iv) Milk (uncertified), namely, milk which has undergone no form of heat-treatment, and is not derived from tuberculosis-free herds, but which attains a certain hygienic standard.

Pasteurization.

The subject of milk pasteurization is much discussed at present. In many of the large cities practically the whole of the milk supplied to the people is pasteurized. In London, about 90% is so treated, and in New York City as much as 99%. In country districts and in the smaller towns, pasteurization is less in evidence. Nearly half of the milk sold in England is sold by producer-retailers; these men are unfavourable to pasteurization, probably on account of the cost of the necessary apparatus. The growing tendency is for the development of big companies, with collective farms and collective marketing, and with large pasteurizing depots.

For pasteurization it is required that the milk should be held at a temperature between 145° and 150° F. for half an hour, and then quickly cooled. The "flash" type of apparatus, much used in America, is not officially approved in England; the milk so treated is not allowed to be designated "pasteurized", but is sold as "bottled milk". In some cities, Birmingham, for instance, sterilized milk is sold: the milk undergoes heat treatment at 212° F. for half an hour.

The British Ministry of Health, in urging the need for proper and efficient pasteurization of milk, point out that much of the so-called pasteurization is by no means satisfactory, and, indeed, deceives the consumer and gives a false sense of security. The Ministry urges local authorities, before licensing pasteurizing plants, to satisfy themselves that the plants are so constructed as to be capable of pasteurizing the milk effectively. When the plant is licensed it should be kept under regular supervision to insure its proper operation. Sir George Newman has said:

The widespread contamination of milk with the organisms of tuberculosis and undulant fever makes it impossible to recommend unreservedly this excellent food unless it has been made safe by efficient pasteurization or boiling.

The Medical Research Council, in its report issued in January, 1934, point out that until bovine tuberculosis can be eradicated, efficient pasteurization remains an essential second line of defence in safeguarding human health. The report states that:

Pasteurization, moreover, gives protection against other diseases derived from cattle, preventing the transmission of bovine streptococcal infection and that of undulant fever. It may be added that the council are not aware of any trustworthy evidence that pasteurization, if properly carried out, has any seriously damaging effect upon the nutritive qualities of the milk.

Dairy Research.

I visited the National Institute for Research in Dairying at Reading (England), and discussed several matters with the Director (Dr. H. D. Kay). The institute is associated with the University of Reading. A farm of 460 acres, with a small herd of cows of the "ordinary mixed" type provides the basis for study. There are an experimental dairy and well-equipped bacteriological and chemical laboratories. The small, but highly-qualified, staff is actively engaged in studying the many problems associated with the production of pure milk.

The bacteriological examination of milk presents many difficulties, and I discussed some of these with Professor Wilson, of the London School of Hygiene and Tropical Medicine. Professor Wilson is a recognized authority on the subject. It is considered that bacteriological counts give only a rough idea of the cleanliness of milk, and no true indication of its likely effects on health. Pasteurized milk is not suitable for ordinary bacteriological count examinations; although bacteria may be present, they are of the thermophilic type, and are not disease-producing. These thermophilic organisms may be present in large numbers in pasteurized milk without being in the least harmful; they are organisms that can withstand a temperature of 145° F.

The big milk-retailing companies in London and other cities insure the purity of their final product by making bacteriological and chemical tests at several stages of the treatment process. I inspected one of the largest pasteurizing plants conducted by United Dairies, at Wormwood Scrubs (London), and was favourably impressed with the efficient methods. The laboratory staff at this depot is devoting special attention to the study of the thermophilic (or thermoduric) bacteria, and methods of controlling them.

Under the aegis of the Medical Research Council, a large amount of work is being done in various research institutions. Methods of immunizing cattle against tuberculous infection are being investigated at the Department of Comparative Pathology at Cambridge; but thus far no

satisfactory method has been found. The staff of the Hannah Dairy Research Institute is studying methods of eradicating tuberculosis from dairy herds, and conducting a large-scale experiment on a series of farms in Ayrshire (Scotland). In its recent report, the Medical Research Council says that:

The whole question of the spread of tuberculosis infection from cattle to man, and of the means by which this may be prevented, is one upon which scientific knowledge is already adequate for more far-reaching practical measures than have yet been attempted. There are certainly matters that are still obscure, but research work has provided a great body of facts upon the main points in the bacteriology and pathology of the disease, and as to methods for its diagnosis, treatment and prevention. The case, therefore, appears to be one in which further action is retarded rather by uncertainty upon economic and administrative points than by lack of scientific information.

(To be continued.)

Correspondence.

HOMOGENEOUS X RADIATION IN BIOLOGICAL EXPERIMENTS.

SIR: In a paper published in THE MEDICAL JOURNAL OF AUSTRALIA on February 2, 1935, I referred to the fact that the failure of overseas workers to obtain evidence of a selective biological action with wave-length had been attributed to the use of insufficiently homogeneous X ray beams. I discussed in some detail the physical methods used to obtain beams of approximately homogeneous X radiation, and concluded that, in certain experiments of Dr. W. Moppett and Dr. W. H. Love, in which the use of approximately homogeneous beams had been given a very special significance, sufficient care had not been taken in applying the methods to justify the beams being described as approximately homogeneous. A reply by Dr. Love, published in THE MEDICAL JOURNAL OF AUSTRALIA on March 9, 1935, contains no evidence to show that those conclusions were unjustified. Two points in that reply, however, appear to me to be of sufficient importance to justify a brief answer.

Dr. Love has completely changed his position regarding the importance he attached to the use of approximately homogeneous radiation in his own experiments. As the paper in which the experiments with the hafnium-filtered radiation are described is possibly not readily available to readers of this journal, may I be permitted to quote some passages from it to indicate the importance Dr. Love then attached to the use of an approximately homogeneous beam? A preliminary review of the literature showed that there was a considerable variation of opinion as to the effect of radiation on living cells, and Dr. Love suggests as one possible explanation that "the employment of heterogeneous radiation makes the accurate determination of the conditions under which any particular biological reaction occurs more difficult. The already complex nature of the biological material demands the maximum simplification of the physical conditions." Describing his own experiments, Dr. Love states that he has "simplified the physical conditions of experiment by using a beam of approximately homogeneous radiation", and later that "it was considered that the use of a monochromatic radiation was likely to enhance the possibilities of correlation and interpretation of experimental results", and that "such a beam was obtained by using a tungsten target in conjunction with a filter of hafnium oxide". It was just these repeated references to the significance of the use of approximately homogeneous and monochromatic radiation which led me to include his paper in a discussion of

some biological experiments, the success of which appeared very definitely to depend upon the degree of homogeneity of the radiation used.

Now, subsequent to my criticism of Dr. Love's method of obtaining approximately homogeneous radiation, he states in his reply that the use of approximately homogeneous radiation was a "superficial condition of experiment which had no essential bearing on the significance ascribed to the experimental results", and that "actually from the significance of these experiments and the results the homogeneity of the beam, approximate or otherwise, does not enter into the story".

Even in adopting this entirely new standpoint, Dr. Love puts forward no experimental evidence of having used both homogeneous and heterogeneous beams to justify his statement that the homogeneity or otherwise of the beam had no significance upon his results.

Dr. Love has charged me with a gross inaccuracy in attributing to him a statement made in a discussion in Canberra on the work of W. Moppett and of C. M. Scott. Neither the official report of the conference nor the report in THE MEDICAL JOURNAL OF AUSTRALIA contain any of Dr. Love's remarks in that discussion.

I can only reply that I made a note of Dr. Love's statement at the meeting, and that in June last I wrote to him asking whether I was correct in thinking that he had stated that Scott's method of obtaining homogeneous radiation was unsatisfactory. To this letter I have received no answer. It is obvious that I had a very reasonable justification for attributing this statement to Dr. Love.

Yours, etc.,

C. E. EDDY.

Natural Philosophy Laboratory,
University of Melbourne,
March 29, 1935.

THE "CHEST" PHYSICIAN AND THE RADIOLOGIST.

SIR: I wish to extend to your correspondent "... Angels Fear to Tread" my deepest sympathy in his conflict with the radiologists. His reiteration of the axiom that the radiological report must be taken with the other findings, especially the carefully collected history, is timely. That the radiograph cannot usurp the microscope is also elementary knowledge. The two reports that are quoted add nothing to the discussion except a laugh. The radiologists need instruction. I might condemn the clinical method by quoting at random from the clinical notes sent to radiologists. And that would make our mirth broddingnagian, without proving anything.

After describing the alterations from normal observed radiologically the report must discuss from that aspect the diagnostic possibilities and probabilities if it is to be helpful. The radiologist is often expected to give information his method can never give and until radiologists learn more pathology and "chest" physicians more radiology it will always be so.

For our benefit perhaps your correspondent will shed his anonymity and translate for us the amusingly absurd reports quoted into their correct form.

Yours, etc.,

F. J. Gwynne.

30, Princes Street,
Auckland,
New Zealand.
April 3, 1935.

SIR: In the issue of March 30 a correspondent ("Angels Fear to Tread") voices a well deserved criticism of the radiologist.

Reports as quoted are the direct result of men specializing in radiology without serving an apprenticeship in general practice; every specialist should have a large clinical experience, and of all the specialties probably that of radiology calls for the widest experience in all branches of medicine and surgery.

The purchase of an X ray unit does not make a radiologist, in spite of the statements of the X ray salesman.

A radiologist should give a report stating the variations from the normal seen in the film, and then enumerate the various pathological conditions which might give these appearances. For routine work this is a very satisfactory procedure, but in more obscure cases a consultation with the medical attendant is desirable.

Some cynics have stated that the radiologist "sees through a glass darkly" and "the positiveness of his opinion is in direct ratio to the obscurity of the glass"; nevertheless all of us who practise our divine art "not frivously" must recognize that the complete collaboration between the medical attendant and the radiologist must surely make more certain a true diagnosis of the pathological conditions.

The days of "conflict" are past and even the most conservative physician recognizes the value of radiographic examination by an expert. From the number of cases seen in the X ray department of a large hospital, which have had no adequate physical examination, one might almost infer that some physicians look upon ordinary clinical methods as obsolete.

In conclusion I might suggest to "Angela, etc." that he may now banish some of his fear and emulate the example of a fellow celestial named Agag.

Yours, etc.,

185, Macquarie Street,
Sydney,
April 5, 1935.

J. G. EDWARDS.

COLOUR BLINDNESS AND TONE DEAFNESS.

SIR: In THE MEDICAL JOURNAL OF AUSTRALIA of April 6, Dr. Harvey Sutton states (apparently, by the context, according to Dr. G. H. Taylor) that the colour blind are never tone deaf and vice versa. This is not so, as I know personally a man of thirty, who, though he has normal visual acuity and hearing, is red-green colour blind and is also tone deaf.

Yours, etc.,

ERIC POCKLEY.

Australasian Pioneers' Club,
Sydney,
April 15, 1935.

THE STUDY OF SURGICAL PATHOLOGY.

SIR: Dr. H. Skipton Stacy's plea for a more intensive study of surgical pathology, in your issue of the 13th instant, is valuable and constructive. It sets out a scheme for the placing of this study on an organized basis by hospital staffs, through the medium of a regular fortnightly meeting at which the clinical and *post mortem* features of all cases coming to autopsy in the hospital are analysed. Such meetings play a great part in raising not only the standards of surgical pathology, but also the keenness and general efficiency of the participating staff members.

I had the privilege of attending many such clinical staff meetings in the United States, where a scheme similar to that outlined by Dr. Stacy has been in vogue in the leading hospitals for many years. It was stimulating to listen, for instance, at the Saturday morning meetings at the Presbyterian Hospital in Chicago, to men of the calibre of Dean Bevan and H. L. Kretschmer, when they traced the history of cases which had been under their care and correlated them with the *post mortem* findings. Additional interest was lent by the fact that all the *post mortem* specimens, fresh from the refrigerator in the autopsy room, were laid out on tables in front of the meeting, together with microscope slides of the various tissues, and accompanied by notes on the pathological findings.

During the past eighteen months regular monthly meetings on the lines outlined by Dr. Stacy have been held by the staff of the Newcastle Hospital. There the

deaths of the preceding month, the *post mortems* and other matters of clinical interest, such as post-operative infections, are discussed, and a report is presented analysing the whole of the medical work for each month. At times the attendance of staff members is disappointing, but to the regular attenders the meetings are full of value. One marked result of the meetings, however, aided by the enthusiasm of the Medical Superintendent (Dr. K. W. Starr), has been the raising of the *post mortem* rate from 6% to 60% of all deaths—a distinct gain in hospital efficiency, and a resultant betterment in the clinical and pathological records. The classification of diseases has also been put on a sound footing in conformity with the best international practice.

Dr. Stacy's scheme is worthy of further attention and emulation by all hospitals where facilities for *post mortem* study are available.

Yours, etc.,

THOMAS HAMILTON,
M.B., Ch.M. (Syd.), F.R.A.C.S., F.A.C.S.,
Honorary Assistant Surgeon.

Newcastle Hospital,
Newcastle,
New South Wales,
April 17, 1935.

Proceedings of the Australian Medical Boards.

QUEENSLAND.

THE undermentioned have been registered, pursuant to the provisions of *The Medical Acts, 1925 to 1933*, of Queensland, as duly qualified medical practitioners:

Birchley, Herbert James, M.B., B.S., 1935 (Univ. Sydney), Brisbane.
Dyring, Valdemar Carl, M.B., B.S., 1926 (Univ. Melbourne), Longreach.
McKellar, Charles Crawford, M.B., Ch.M., 1926 (Univ. Sydney), F.R.C.S. (Edinburgh), 1934, Ipswich.

Obituary.

ELMER I. MCKESSON.

A FORMER pupil of Dr. Elmer I. McKesson, the well known American anaesthetist, who died on February 22, 1935, writes:

In the passing of Elmer I. McKesson, America loses one of her most eminent anaesthetists. For thirty years he has been known as a master anaesthetist, a research worker, an inventor of genius and a teacher of anaesthesia. He has held high office amongst the Associated Anaesthetists of the United States and Canada and in the International Anesthesia Research Society.

McKesson designed apparatus of unsurpassed refinement, both for anaesthesia and the therapeutic use of gases, and used it to full advantage. Indeed, his technical mastery and his admirable appliances led him sometimes to employ methods unsuited to anaesthetists of lesser skill. Of this, his advocacy of "secondary saturation" and the intricate technique which delayed until relatively late his adoption of endotracheal methods, are cases in point. His achievement, however, lay in the education of the American surgical public in the advantages of gas anaesthesia and in the invention of apparatus well designed to reveal those advantages.

As a teacher his method was practical instruction under supervision, combined with informal lectures upon basic physiology. Clinical anaesthesia, to him, was ever the gateway to clinical research. As a man he was genial and

kindly. His influence upon the anaesthetic thought of the day will survive him. His personality as man and teacher will be long remembered by the many British graduates who have been his guests and pupils.

TESTIMONIAL TO MR. GEORGE MACDONALD.

MR. GEORGE MACDONALD, Chief Laboratory Assistant in the Department of Pathology in the University of Sydney, now finds the strain of the work too great for his health and is reluctantly compelled to retire. For the last thirty-three years he has worked with the Professor of Pathology—for the first five years at the Royal Prince Alfred Hospital and for the last twenty-eight years at the University.

All graduates and students of medicine who passed through the Department of Pathology during those years, particularly when bacteriology and pathology were taught as one subject, will retain grateful memories of Mr. Macdonald's never-failing courtesy and ever-ready help. If any should wish to mark their appreciation of his work by a parting gift, subscriptions may be sent to Dr. A. S. Walker, to Dr. Keith Inglis, to Professor D. A. Welsh, or to the Editor of THE MEDICAL JOURNAL OF AUSTRALIA. Subscriptions will be acknowledged in these columns.

Books Received.

- CLIO MEDICA: A SERIES OF PRIMERS ON THE HISTORY OF MEDICINE**, edited by E. B. Krumbhaar, M.D.; XIII: German Medicine, by W. Haberling, M.D., translated by J. Freund, M.D.; 1934. New York: Paul B. Hoeber. Folio, pp. 172, with nine illustrations. Price: \$1.50 net.
- CLIO MEDICA: A SERIES OF PRIMERS ON THE HISTORY OF MEDICINE**, edited by E. B. Krumbhaar, M.D.; XIV: Medicine in Persia, by C. Elgood, M.D., M.R.C.P.; 1934. New York: Paul B. Hoeber. Folio, pp. 118, with illustrations. Price: \$1.50 net.
- A SHORT PRACTICE OF SURGERY**, by H. Bailey, F.R.C.S., and R. J. McM. Love, M.S., F.R.C.S.; Second Edition; 1935. London: H. K. Lewis and Company Limited. Demy 8vo., pp. 996, with 731 illustrations, of which 83 are coloured. Price: 30s. net.

Diary for the Month.

- MAY 6.—New South Wales Branch, B.M.A.: Organization and Science Committee.
- MAY 7.—Tasmanian Branch, B.M.A.: Council.
- MAY 10.—Queensland Branch, B.M.A.: Council.
- MAY 14.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
- MAY 14.—Tasmanian Branch, B.M.A.: Branch.
- MAY 15.—Western Australian Branch, B.M.A.: Branch.
- MAY 15.—Victorian Branch, B.M.A.: Clinical Meeting.
- MAY 21.—New South Wales Branch, B.M.A.: Ethics Committee.
- MAY 21.—Tasmanian Branch, B.M.A.: Council.
- MAY 22.—Victorian Branch, B.M.A.: Council.
- MAY 23.—New South Wales Branch, B.M.A.: Clinical Meeting.
- MAY 24.—Queensland Branch, B.M.A.: Council.
- MAY 28.—New South Wales Branch, B.M.A.: Medical Politics Committee.
- MAY 30.—South Australian Branch, B.M.A.: Branch.
- MAY 30.—New South Wales Branch, B.M.A.: Branch.
- MAY 31.—Queensland Branch, B.M.A.: Bancroft Memorial Lecture.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, locum tenentes sought, etc., see "Advertiser", pages xvi-xviii.

- CHILDREN'S HOSPITAL (INCORPORATED), PERTH, WESTERN AUSTRALIA:** Junior Resident Medical Officer.
- PUBLIC SERVICE COMMISSIONER, ADELAIDE, SOUTH AUSTRALIA:** Resident Medical Officer.
- REPATRIATION COMMISSION, BRISBANE, QUEENSLAND:** Resident Medical Officer.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.I.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 125, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phoenix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Brisbane Associate Friendly Societies' Medical Institute. Chillagoe Hospital. Members accepting LODGE appointment and those desiring to accept appointments to any COUNTRY HOSPITAL, are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	Officer of Health, District Council of Elliston. All Lodge Appointments in South Australia. All Contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 205, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (Wellington Division): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Editorial Notices.

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